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A.M.A. ARCHIVES OF SURGERY

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1. Spencer, H.; Berger, E.; Charles, M.; Gottesman, E. D., and Laszlo, D.: Effects of 17-alpha-Ethyl-17-Hydroxy-Norandrostenone, Proc. Am. A. for Cancer Res. *2*:149 (April) 1956.

2. Proceedings of a Conference on the Clinical Use of Anabolic Agents, Chicago, Illinois, Searle Research Laboratories, April 9, 1956.

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TABLE OF CONTENTS

VOLUME 76 MARCH 1958 NUMBER 3

ORIGINAL ARTICLES

PAGE

Localization of Stomach Ulcers
C. A. Helkwig, M.D.; J. W. Welch, M.D., and P. N. Wilkinson, A.B., Halstead, Kan. 331

Technique and Results of Isolation of Cancer Cells from the Circulating Blood
Stuart Roberts, M.D.; Alvin Watne, M.D.; Ruth McGrath, B.S.; Elizabeth McGrew, M.D., and Warren H. Cole, M.D., Chicago 334

Subarachnoid Alcohol Block in the Management of Pain of Malignant Disease
D. M. Perese, M.D., Buffalo 347

Ischemia of the Left Colon Associated with Abdominal Aortic Aneurysms and Their Treatment
John McKain, M.D., and Harris B. Shumacker Jr., M.D., Indianapolis 355

Endobronchial Hamartoma
Thomas W. Shields, M.D., and Thomas E. Lynn, M.D., Chicago 358

Biliary Dyskinesia in T-Tube Cholangiography
Joseph Hodge, M.D.; Claude Barrick, M.D., and Edward McLaughlin, M.D., Philadelphia 361

Potassium, Magnesium, and Neostigmine for Controlled Cardioplegia
Doris M. H. Merritt, M.D.; Will C. Sealy, M.D.; W. Glenn Young Jr., M.D., and Jerome S. Harris, M.D., Durham, N. C. 365

Reconstruction of the Amputated Thumb
I. K. Mikhail, M.D., F.R.C.S., Dhahran, Saudi Arabia 372

Prevention of Nonhemolytic Blood Transfusion Reactions with an Antihistamine, Chlorpheniramine
Frederick M. Offenkrantz, M.D., Cranford, N. J., and George Babcock Jr., M.D., Rahway, N. J. 379

Superior Vena Caval Replacement
Angelo Riberi, M.D., and Thomas C. Moore, M.D., Indianapolis 384

A Histologic Study of the Tissues Surrounding Experimental Nylon Aortic Substitutes
William O. Barnett, M.D., and Tom D. Norman, M.D., Jackson, Miss., with the Technical Assistance of Carolyn Anderson, M.T., A.S.C.P. 389

Effect of Intravenous Nutrient Solutions on Ventricular Fibrillation in the Hypothermic Dog
Leonard J. Caranna, M.S.; François J. P. Telmosse, M.D., and Henry Swan, M.D., Denver 394

Primary Resection of Descending Colon for Obstructing Annular Carcinoma
Edward A. Fitch, M.D., and Frank R. Denman, M.D., Houston, Texas 398

Intrathoracic Tension Phenomena in the Neonatal Period and Infancy
Joseph W. Gilbert Jr., M.D., and Richard T. Myers, M.D., Winston-Salem, N. C. 402

Thyroid Carcinoma and Nodular Goiter in a Community Hospital
Charles D. Hershey, M.D., Wheeling, W. Va. 407

Obstruction of the Small Intestine Caused by Acute Cholecystitis
George L. Hoffmann Jr., M.D.; Klaus F. L. von Kessel, M.D., and Stanley O. Hoerr, M.D., Cleveland 412

Instrument to Assist in the Surgical Removal of Stones from the Bile Ducts
James F. O'Neill, M.D.; Paul R. Casey, M.D., and John P. McCafferty, M.D., Philadelphia 414

Stricture of the Trachea Following Traumatic Fracture
Julian K. Quattlebaum Jr., M.D., Savannah, Ga. 417

Intra-Arterial Pressure Studies in Peripheral Arterial Reconstructions
Worthington G. Schenk Jr., M.D., and James G. Stephens, M.D., Buffalo 424

Clinical Aspects and Management of Sacrococcygeal Teratoma
Bernard Seidenberg, M.D., and Elliott S. Hurwitt, M.D., New York 429

An Anesthetic Technique for Cardiac Surgery Which Utilizes 100% Oxygen as the Only Inhalant
Philip Bailey, M.D.; Frank Gerbode, M.D., and Laurens Garlington, M.D., San Francisco 437

Studies on the Site and Mechanism of Gastrin Release
Clarence M. Baugh, M.D.; Jose L. Bravo, M.D.; Jaime Barcena, M.D., and Lester R. Dragstedt, M.D., Ph.D., Chicago 441

Gastrectomy Complicated by the Guillain-Barré Syndrome
David Orringer, M.D., Pittsburgh 447

Indications and Uses for Gastrostomy Tube Suction in Surgery of the Upper Abdomen
Frank A. Rogers, M.D., Whittier, Calif. 451

Use of Randall Forceps in Bile Duct Surgery
Robert S. Sparkman, M.D., Dallas, Texas 455

Autotransplantation of the Lingual Thyroid
Henry Swan, M.D.; Dalton Jenkins, M.D., and Charles Macgregor, M.D., Denver 458

(Continued on next page)

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VOLUME 76 MARCH 1958 NUMBER 3

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TABLE OF CONTENTS (Continued)

CASE REPORTS

Removal of a Foreign Body in the Rectosigmoid Using a Tonsil Snare
Edward J. Carry, M.D., Whipple, Ariz. 465

Angular Dermoids
E. L. Marston, M.D., and Ralph W. Bland, M.D., Winston-Salem, N. C. 467

Radical Mastectomy for Carcinoma of the Breast During Pregnancy
David M. Weeks, M.D., New York 469

Carcinoma in Chronic Ulcerative Colitis
Benjamin B. Jackson, M.D., Louisville, Ky.; Harold G. Olken, M.D., Lynn, Mass., and S. Peter Sarris, M.D., Boston 472

CORRESPONDENCE

In Vitro Oxygenation of Fresh Whole Blood for Arterial Perfusion
Ivan W. Brown Jr. M.D., and W. Glenn Young, M.D., Durham, N. C. 475

Possible Etiology of Ainhum
C. M. Lee Jr., M.D., Boston 475

SURGERY ILLUSTRATED

Some Complications of Circumcision and Their Surgical Repair
Louis T. Byars, M.D., St. Louis, and Lt. Comdr. William C. Trier (MC), U. S. N. 477

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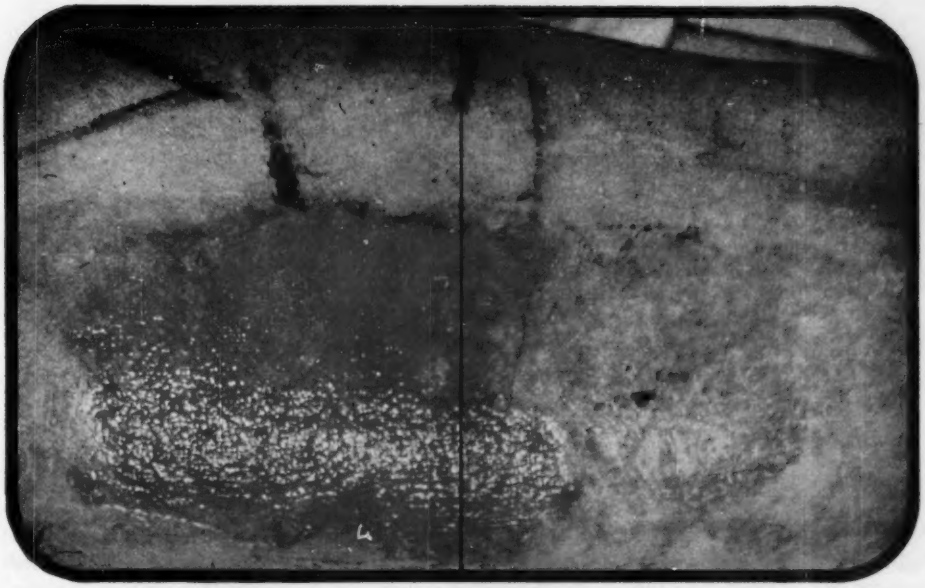

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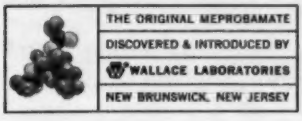

REFERENCES:

1. *Rushia, E. L.: Preliminary report on the use of meprobamate for pre-anesthetic sedation. J.M.A. Georgia* **46**:*93, March 1957.*
2. *Lamphier, T. A.: The role of meprobamate in postoperative surgical care. Ann. New York Acad. Sc.* **67**:*810, May 9, 1957.*
3. *Kern, E. C.: Preoperative sedation with meprobamate (Miltown) in surgery of eye, ear, nose and throat. Eye, Ear, Nose & Throat Month.* **36**: *408, July 1957.*

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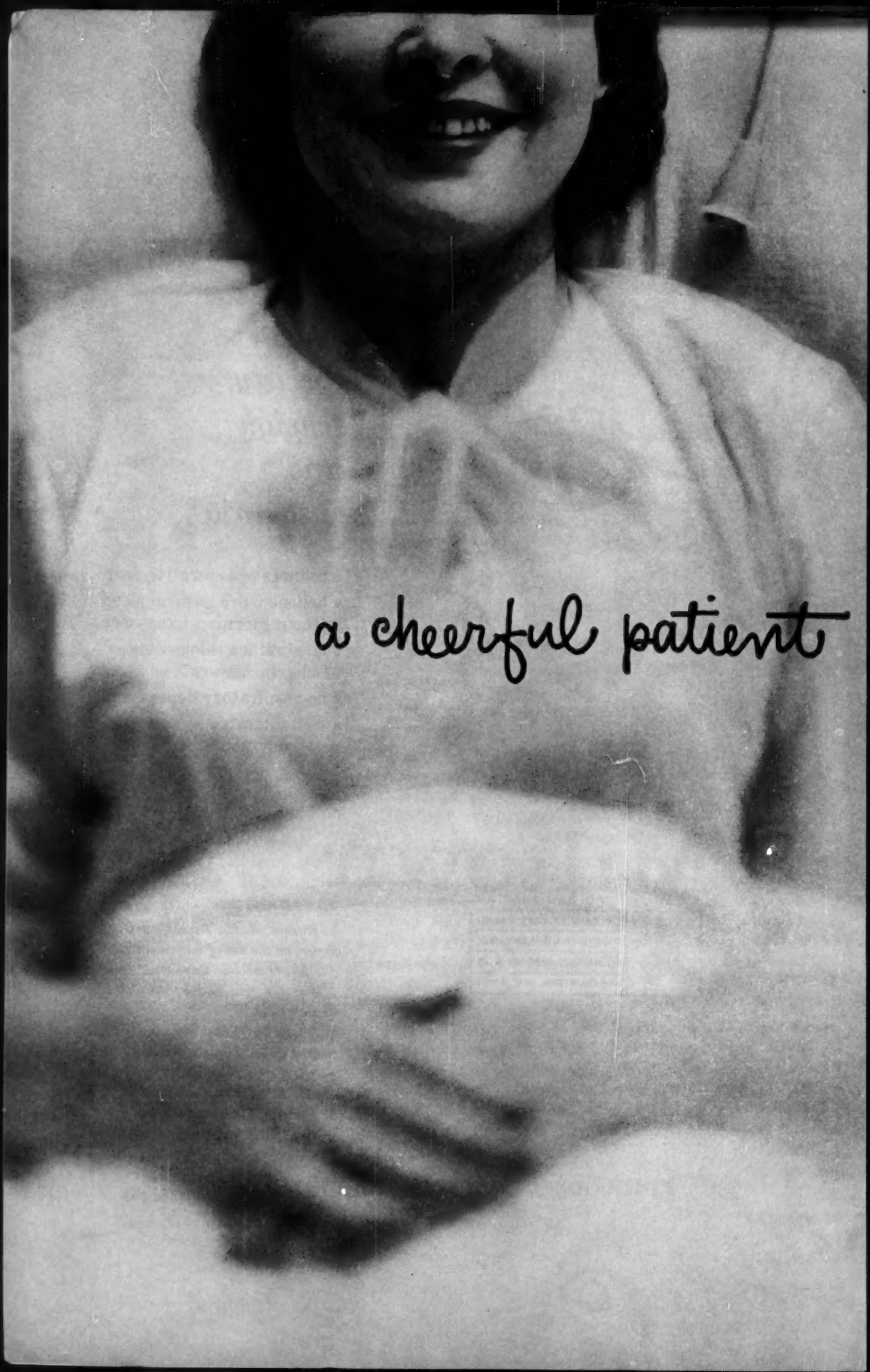
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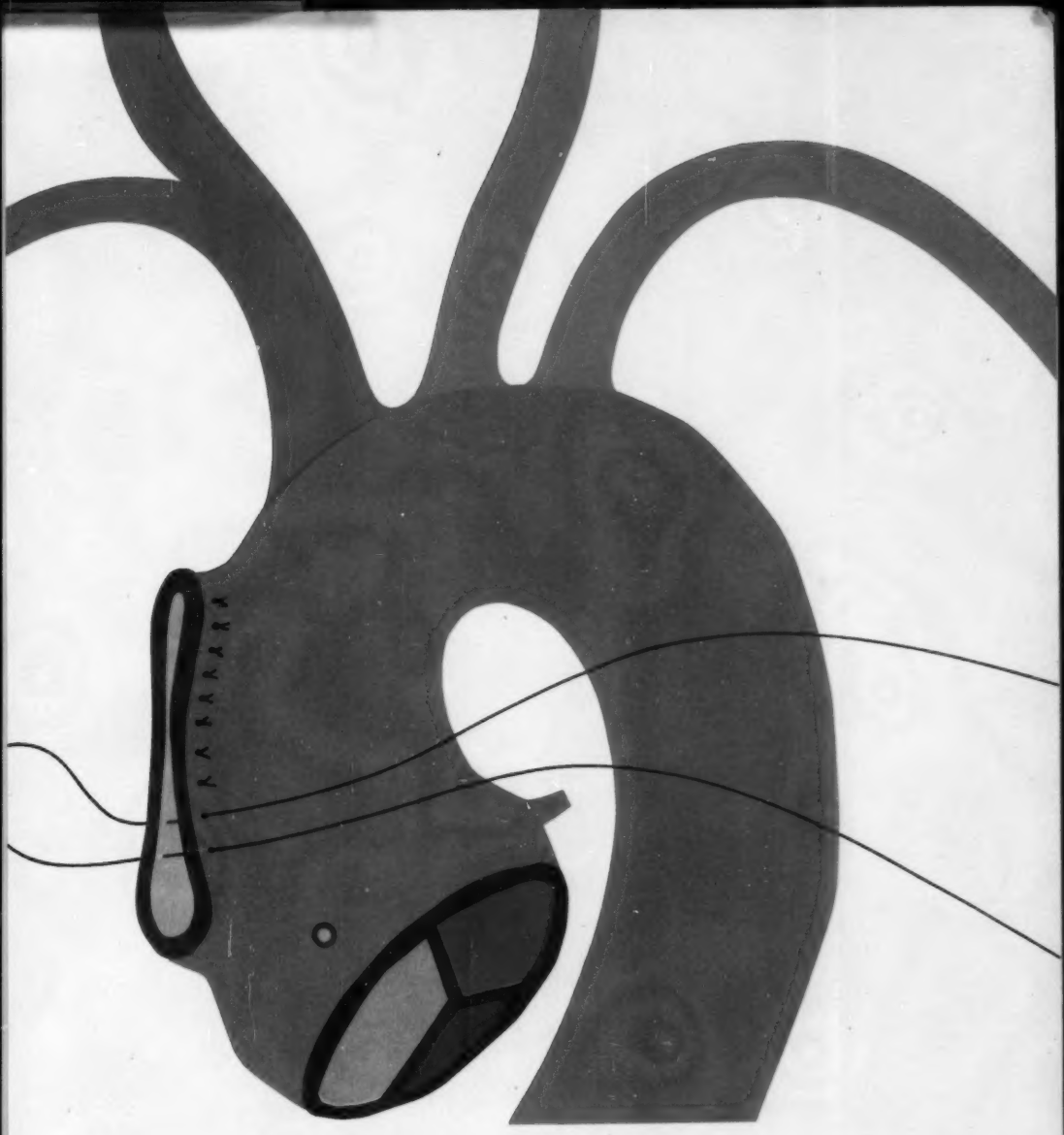

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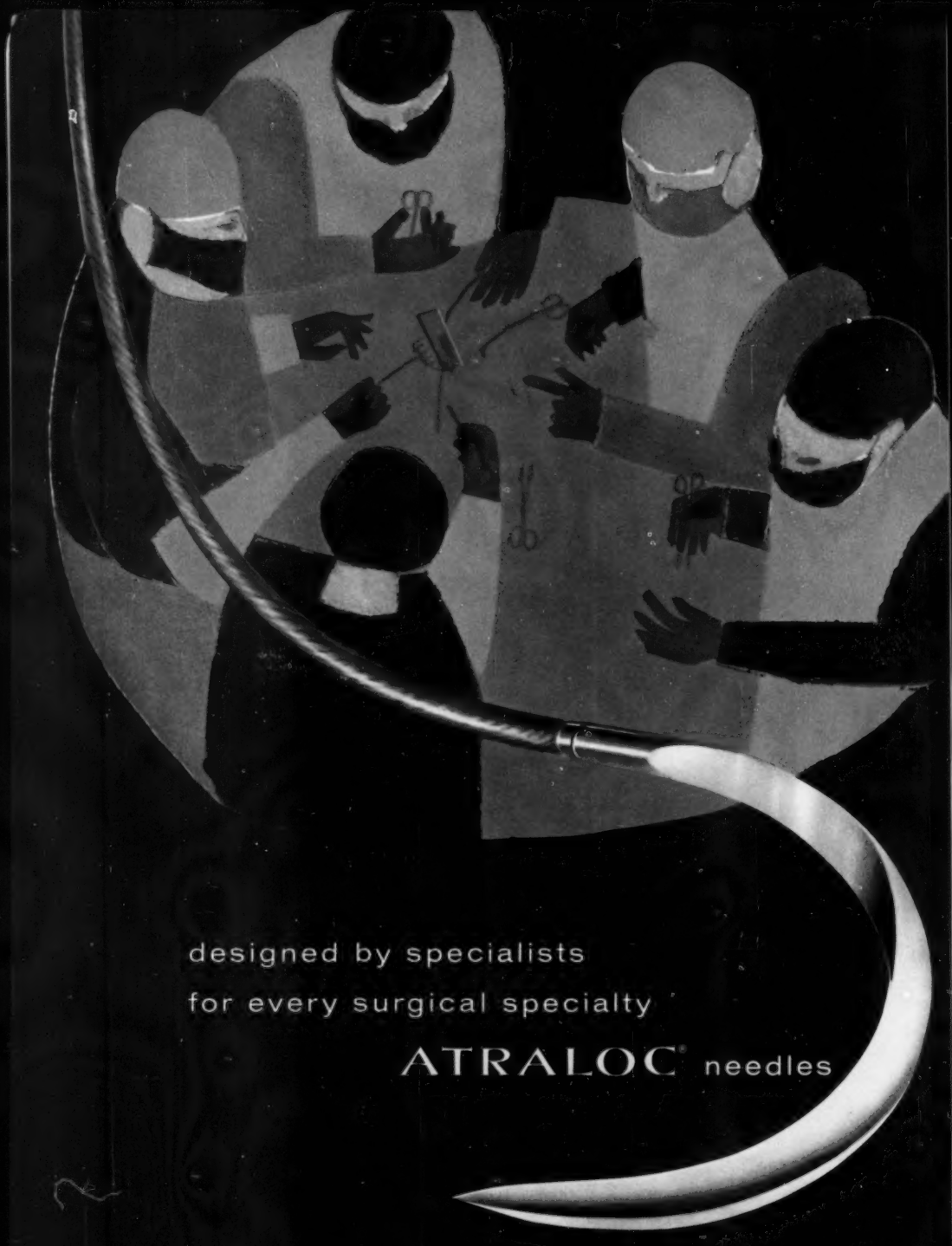

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Localization of Stomach Ulcers

C. A. HELLWIG, M.D.; J. W. WELCH, M.D., and P. N. WILKINSON, A.B., Halstead, Kan.

More than 100 years ago (1829) Cruveilhier [4] made the observation that chronic gastric ulcers are usually situated at the lesser curvature. This has been confirmed by many writers, but no valid explanation for this peculiar localization has come forward.

There is strong evidence (Bolton [2] and Konjetzny [9]) that chronic gastric ulcers arise from acute ulcers. Thus two problems present themselves: first, the cause of acute ulcers, and, second, the factors which lead to the persistence or nonhealing of ulcers. Acute ulcers are found not only at the lesser but also on the greater curvature, and at the cardia as well as in the fundus (Stewart [15]). Their etiological factors—chemical, hormonal, neurological, and psychological—have been widely discussed in modern treatises. However, very little attention has been given to the second problem: Why ulcers at the lesser curvature become chronic. The peculiar localization of almost all chronic stomach ulcers at the lesser curvature is the great stumbling block in the understanding of gastric ulcers (Boyd [3]).

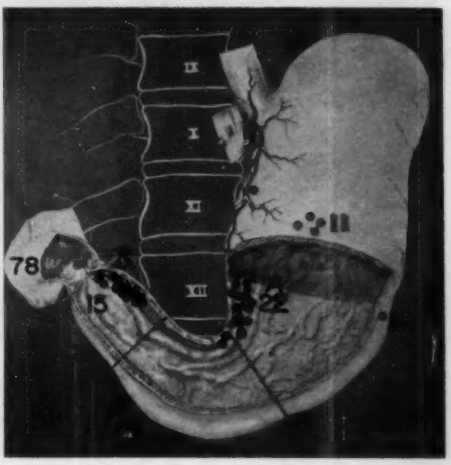
Material and Methods

One hundred twenty-seven specimens obtained by subtotal gastric resection at the Hertzler Clinic were studied before fixation in formalin; each stomach was photographed, and the exact site of its ulcer was entered into a schematic drawing of a stomach (Fig. 1). There were 49 gastric ulcers and 78 duodenal ulcers. By microscopic examination the clinical diagnosis of benign chronic ulcer was confirmed. Acute ulcers and healed ulcers were not included in the present study.

Results

All chronic gastric ulcers except one were situated at the lesser curvature. Twenty-two were found proximal to the incisura angularis; two were in the antrum, and 15 in the pyloric canal. We found only one gastric ulcer in the greater curvature. There were, near the lesser curvature, four ulcers in the anterior wall and seven in the poste-

Fig. 1.—Localization of chronic gastric ulcers. All gastric ulcers except one were situated at or near the lesser curvature. Only two areas were involved, *A* proximal to the incisura and *B* near the pylorus.



Submitted for publication July 24, 1957.

The material on which this paper is based was presented as part of a scientific exhibit of the Section on Pathology and Physiology at the 106th Annual Meeting of the American Medical Association, New York, June 3-7, 1957.

rior wall (Fig. 1). It is evident that ulcers do not occur in the whole length of the lesser curvature but only in two areas, i. e., proximal to the incisura and near the pylorus.

The common theory, that the food passing along the *Magenstrasse* prevents the healing of an ulcer by mechanical irritation, is not substantiated by our observation that only two points of the pathway of the stomach are affected by chronic ulcer. Also, the often-repeated statements, that the ingested barium, after entering the stomach, runs along the lesser curvature, the so-called *Magenstrasse,* is not based on fact. As one observes the barium entering the stomach on the fluoroscope, it is seen to flow downward in almost every direction, filling the whole stomach cavity.

We believe that Figure 2 gives the explanation for the peculiar localization of chronic gastric ulcers. This roentgenogram of a normal stomach was taken with the patient in prone position. The part in front of the vertebral column appears empty, the barium meal having been displaced by the vertebral column. The two regions of the lesser curvature which are the common sites of stomach ulcer (Fig. 1) correspond to the lateral walls of the vertebral column. The latter forms a rigid, jetty-like protrusion against which the gastric contents strike rhythmically during the stomach contractions. Any ulcer located in these two regions will be subjected to a great deal of buffeting; thus its healing will be prevented. The delaying effect of repeated injury on healing is known to every child with a grazed knuckle (Illingworth [7]).

Fig. 2.—Roentgenogram of normal stomach with patient in prone position. The jetty-like protrusion of the vertebral column has displaced the barium meal in front of the vertebra. The two areas of predilection for chronic gastric ulcers (*A* and *B*) correspond to the left and right walls of the vertebrae, respectively.

In the literature some observations are reported which support the theory that mechanical factors play an important role in the nonhealing of gastric ulcers. According to Aschoff [1] (1924), losses of mucosa in the *Magenstrasse* continue gaping, and are more injured mechanically by the peristaltic movements than in other parts of the stomach. Redwitz and Fuss [13] (1928) suggested that the liver, pancreas, vertebral column, and aorta may contribute to the pathogenesis of gastric ulcer by compressing the midportion of the stomach.

Hansen [6] found that the incidence of gastric ulcer in kyphoscoliosis is almost three times as frequent as in general. Rasmussen,[12] Schütz,[14] and Lehmann [10] observed before the turn of the century that stomach ulcers were more frequent in women than in men. They attributed this fact to compression of the stomach by tight corsets. The decreasing incidence of stomach ulcers in women was explained by Hansen by the decline of the fashion of tight lacing. Einhorn [5] (1928) stated that ulcer patients who wore suspenders improved more readily than those wearing belts.

Illingworth explained persistence of ulcers by stretching and tearing of the lesser curvature during gastric peristalsis. Coarseness of food is regarded as responsible for persistence of gastric ulcers by Aschoff, Illingworth, and others. Illingworth feels that the most important consideration in diet

for ulcer patients is the prevention of trauma: "Whatever its constituents, the food should always be liquid or in puree form." Ivy [8] demonstrated in rabbits and cats that mechanical irritation delayed healing of experimental gastric ulcers.

The influence of the upright position on the persistence of ulcers points also to a mechanical factor. It is well known that chronic ulcers hardly ever occur in quadrupeds and that experimental ulcers in animals heal in a short time. Lorber and Shay [11] (1954) observed a much higher intragastric pressure in the standing and sitting position than in the supine. Ingestion of a water-barium mixture with the patient sitting resulted in an appreciable rise in intragastric pressure, whereas only little change in pressure was noted when the patient was in the supine position.

Clinical experience is in agreement with these experimental data, for the horizontal, as opposed to the upright, position is the quickest and most certain way to lasting relief from ulcer symptoms (Illingworth).

Summary and Conclusions

While it has been known for more than 100 years that chronic stomach ulcers are situated commonly at the lesser curvature, there is no agreement about the cause of this peculiar localization.

A study of 127 stomach specimens with peptic ulcer revealed that, as a rule, only two areas of the lesser curvature are involved in the gastric ulcer process, proximal to the incisura angularis and near the pylorus.

These two areas of the lesser curvature are adjacent to the lateral wall of the vertebral column.

The waves of gastric contents strike these two regions of the stomach wall rhythmically against the jetty-like, rigid protrusion of the vertebral column.

Acute ulcers situated in one of these two areas will be subjected to repeated mechanical injury and their healing will be prevented.

Dr. E. N. McCusker, radiologist to the Hertzler Clinic, made the roentgenogram (Fig. 2).

The Hertzler Clinic.

REFERENCES

1. Aschoff, K. A. L.: Lectures on Pathology, New York, Paul B. Hoeber, Inc., 1924, p. 279.

2. Bolton, C.: Ulcer of the Stomach, London, E. Arnold, 1913.

3. Boyd, W.: The Pathology of Internal Diseases, Ed. 5, Philadelphia, Lea & Febiger, 1950, p. 271.

4. Cruveilhier, J.: Anatomie pathologique du corps humain, ou descriptions avec figures lithographiées et coloriées, des diverses altérations morbides dont le corps humain est susecptible, Paris, J.-B. Baillière, 1829-1835, Vol. 1.

5. Einhorn, M.: Suspenders vs. Belts in Treatment of Gastric and Duodenal Ulcers, Am. J. M. Sc. 175:395-404, 1928.

6. Hansen, J. L.: Aendringer i ulcussygdommens fremtraeden, Copenhagen, Ejnar Munksgaards Forlag, 1943.

7. Illingworth, C. F. W.: Peptic Ulcer, Edinburgh & London, E. & S. Livingstone, Ltd., 1953.

8. Ivy, A. C.; Grossman, M. I., and Bachrach, W. H.: Peptic Ulcer, New York, The Blakiston Company (Division of Doubleday & Company, Inc.), 1950.

9. Konjetzny, G. E.: Die entzündliche Grundlage der typischen Geschwürsbildung im Magen und Duodenum, Berlin, Springer-Verlag, 1930.

10. Lehmann, H.: Ein Beitrag zur Frage der Frequenz und Localization des Ulcus pepticum ventriculi et duodeni, Mitt. Grenzgeb. Med. u. Chir. 39:185-204, 1926.

11. Lorber, S. H., and Shay, H.: Technical and Physiological Considerations in Measuring Gastro-Intestinal Pressures in Man, Gastroenterology 27: 478-487, 1934.

12. Rasmussen, A. F.: Über die Magenschnürfurche und die Ursache des chronischen Magengeschwürs, Centralbl. med. Wissensch. 25:162, 1887.

13. von Redwitz, E., and Fuss, H.: Die Pathogenese des peptischen Geschwürs des Magens und der oberen Darmabschnitte, Stuttgart, F. Enke, 1928.

14. Schütz, E.: Das tiefgreifende Magengeschwür, Arch. Verdauungskr. 23:105, 242, and 317, 1916-1917.

15. Stewart, M. J.: The Pathology of Gastric Ulcer, Brit. M. J. 2:955-957; 1021-1025, 1923.

Technique and Results of Isolation of Cancer Cells from the Circulating Blood

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The invasion of veins by many malignant tumors has been shown by numerous investigators,[1-4] but reports of the actual cytologic demonstration of cancer cells in the circulating blood have been relatively few,[5,6] due to the technical difficulty in the separation and identification of the few cancer cells from the numerous formed elements of the blood. This study is a continuation of work begun four years ago[7] and concerns the technique for the isolation of cancer cells from the blood and the occurrence of these cancer cells in the circulating blood, including the changes wrought by the manipulation incident to surgery.

Historical Review

Demonstration of Cancer Cells in Venous Blood.—In 1869, Ashworth[8] found cells in the blood which were of the same size and appearance as those of the patient's multiple malignant skin tumors. Schleip,[9] in 1906, described cells varying from the normal in a case of gastric carcinoma. In the same year, Aschoff[10] reported myeloma cells in the postmortem blood of a patient with myelomatosis. Ward,[11] in 1906, reported numerous large cells, presumed to be tumor, in the peripheral blood from a patient with gastric cancer a few hours before death. In 1919, Marcus[12] reported "abnormal cells" in the blood taken from the finger of a patient with bronchogenic carcinoma five hours prior to death. In 1921, Quensel[13] examined the blood of 50 cadavers with malignant tumors, finding malignant-appearing cells in 6 cases, 4 of which were of gastric carcinoma.

One of the first systematic studies of living patients was done by Pool and Dunlop[5] in 1934, in which they examined the peripheral blood of 40 patients having cancer. They reported atypical cells in the blood in 17 of the 40 cases, but were uncertain that these were cancer cells. They were also the first to mention obtaining blood from the mesenteric vein of a patient undergoing surgery for carcinoma of the sigmoid colon, but the results of this study were not reported.

Utilizing the Papanicolaou stain, Cole, Packard, and Southwick,[7] in 1954, demonstrated cancer cells in the fluid perfused through the major artery and collected from the vein of a colonic specimen containing carcinoma. In 1955, Fisher and Turnbull[14] reported tumor cells recovered from the blood of the major mesenteric venous channels in 8 of 25 (32%) specimens of colorectal carcinoma.

In a detailed study of the subject, Engell[6] (1955) reported tumor cells in the venous blood draining the tumor area during surgery in 63 (59%) of 107 cases of colorectal carcinoma, 6 (75%) of 8 cases of gastric cancer, 3 (75%) of 4 cases of lung cancer, and 3 (75%) of 4 cases of breast cancer. Also, he found tumor cells in the peripheral blood in 10 (13%) of 79 cancer patients during surgery and in 7 (50%) of 14 cases of advanced, inoperable carcinomas. He found no relationship to surgical manipulation.

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The staining technique and criteria for interpretation of this material are those described in Papanicolaou, G. N.: Atlas of Exfoliative Cytology, Cambridge, Mass., Harvard University Press, 1954.

Recently, Moore [15] reported tumor cells in the venous blood draining the tumor area during surgery in 60 (55%) of 109 cases of carcinoma and in the peripheral blood of 93 (52%) of 179 cases. The last figure includes both operable and inoperable cases of lung, breast, and gastrointestinal tract carcinomas.

Separation of Cell Population of Blood.

Prior to 1946, methods for separating leukocytes from whole blood had been by the hemolysis of red cells with organic acids or saponin, or by collecting the "buffy layer" when citrated whole blood was centrifuged.

In studies on malarial blood, Ferrebee and Geiman,[16] in 1946, described the separation of parasitized erythrocytes from normal erythrocytes, using a method which took advantage of the difference in their specific gravity. The malarial whole blood was layered onto a solution of plasma albumin of high specific gravity. After centrifugation, normal red blood cells, having a specific gravity greater than that of the albumin, were packed at the bottom of the tube, while the lighter, infected cells remained suspended at the interface between plasma and albumin.

The application of the same physical principle was successfully employed by Vallee, Hughes, and Gibson,[17] in 1947, to effect separation of leukocytes from whole blood.

In 1950, following the lead that the separation of cell types in mixed populations was feasible by taking advantage of small differences in their specific densities, Fawcett, Vallee, and Soule [18] were successful in separating cancer cells from bloody peritoneal and pleural serous fluids. This technique was utilized by McGrew [19] for the concentration of cancer cells from body fluids for cytologic study.

Another approach to the separation of leukocytes from erythrocytes was thoroughly investigated by Buckley, Powell, and Gibson [20] in 1950. In this method, fibrinogen was added to whole blood, causing rouleaux formation of the erythrocytes, with their rapid sedimentation, leaving the leukocytes and other nucleated elements in the supernatant plasma. A similar principle was utilized by Li and Osgood,[21] who added phytohemagglutinin from red beans to whole blood, causing agglutination of erythrocytes and hence their accelerated sedimentation.

Technique of Cancer Cell Isolation

*Preparation of Stock Albumin Solution.**

The albumin is Armour's "Fraction V, reworked," crystallized bovine albumin. Fraction V as normally prepared cannot be used for this purpose because of its high salt content. "Fraction V, reworked," contains a lower salt content. A 35% solution is prepared by dissolving 100 gm. of "Fraction V, reworked," crystallized bovine albumin in distilled water and brought to a volume of 285 cc.

The pH of this solution is then adjusted by adding sodium bicarbonate and applying a vacuum to remove carbon dioxide for approximately eight hours, or until the pH has risen from the original of 5.1 to 7.4, as measured by the Beckman glass electrode. Lot #P-13403 has required 8.8 mg. of sodium bicarbonate per cubic centimeter.

The sodium bicarbonate added to adjust the pH of the solution may not produce the desired osmolarity, as measured by the freezing-point depression method, using a Fiske osmometer. Therefore, sodium chloride is added until the freezing point is depressed to −0.5208 C, which is the measurement for 280 milliosmoles, physiologic ranges being from 280 to 285 milliosmoles. Lot #P-13403 has required 3.97 mg. of sodium chloride per cubic centimeter.

The specific gravity of this albumin stock solution thus prepared will be approxi-

* The albumin solution is being prepared to meet the proper specifications by the Pentex Corporation, Kankakee, Ill. If this preparation meets specifications, the adjustments under "Preparation of Stock Albumin Solution" will already have been made.

mately 1.092±0.003, as measured by a hydrometer.

The albumin stock solution may be stored in rubber-stoppered 50 cc. bottles and kept under refrigeration at 4 C. The pH has remained constant for as long as two months.

Adjustment of Stock Albumin Solution to Various Specific Gravities.—Different specific gravities are produced by diluting the albumin stock solution with isotonic sodium chloride solution. The density of the particular dilution is calculated from the following formula[22]:

$$D=\frac{Da\ Va+Db\ Vb}{Va+Vb}$$

Where D=the specific gravity desired
Da=the specific gravity of the albumin stock solution
Va=the volume of albumin added
Db=the specific gravity of the isotonic saline
Vb=the volume of saline which must be added

Possible small differences between the total volume and Va+Vb are neglected.[22]

Preparation of Stock Fibrinogen Solution.†—The fibrinogen is Armour's Fraction I. The material is supplied as a powder, containing about 60% protein, of which 60% is reported as clottable, and 40% is citrate salt by dry weight. Accordingly, 400 mg. of the material contains approximately 160 mg. of citrate salts and 240 mg. of protein, of which about 140 mg. is fibrinogen.

The fibrinogen solution is prepared by dissolving 400 mg. of the dry powder in 10 cc. of distilled water, which would then contain approximately 140 mg. of fibrinogen. This stock solution is hypotonic and acidic and therefore requires the addition of sodium bicarbonate and sodium chloride to achieve isotonicity and a pH of 7.4. Lot #R3612 has required 15 mg. of sodium bicarbonate and 30 mg. of sodium chloride for this volume of fibrinogen solution. A vacuum is applied for five minutes to remove carbon dioxide.

Adjustment of Stock Fibrinogen Solution to Various Concentrations.—Various concentrations are prepared by adding isotonic sodium chloride solution to the stock fibrinogen solution, utilizing the formula of Buckley et al.[20]

$$f=F(1.00-H_2)W_2-3(1.00-H_1)W_1 \quad (1)$$

f=total fibrinogen, in milligrams, in all of the diluent.
F=concentration of fibrinogen, in milligrams per cubic centimeter of plasma-Fraction I mixture. Following the addition of fibrinogen to the blood sample, the erythrocytes settle, and the supernatant is referred to as the plasma-Fraction I mixture. Buckley[20] has shown that the optimum concentration of fibrinogen in the plasma-Fraction I mixture is 6.0 to 7.0 mg., for which we use 6.7 mg.
H_2=hematocrit of diluted blood. The optimum hematocrit for separation is in the range of 24% to 30%,[20] for which we use 27%.
W_2=volume of the diluted blood, in millimeters. This is determined by dividing the volume of RBC of the whole blood by the hematocrit of the diluted blood.
3=the assumed number of milligrams of fibrinogen per cubic centimeter of normal human plasma.
H_1=hematocrit of the whole blood.
W_1=volume of the whole blood, in milliliters.

Example: Ten cubic centimeters of blood is drawn from a patient whose hematocrit is 40%. Substituting in formula (1) value for $W_2=\frac{4\text{ cc.}}{0.27}=14.8$ cc.

$$f=6.7(1.00-0.27)14.8-3(1.00-0.40)10$$
$$=6.7(0.73)14.8-3(0.60)10$$
$$=72.39-18.00$$
$$f=54.39 \text{ mg. in all of the diluent.}$$

Therefore, 3.8 cc. of Fraction I solution, which contains 14 mg. of Fraction I per cubic centimeter, is required to furnish 54.39 mg. of fibrinogen, giving a total volume of only 13.8 cc. Therefore, 1 cc. of isotonic sodium chloride solution is added to bring the total volume of the diluted blood to 14.8 cc., or a hematocrit of 27%.

Collection of Blood Samples.—Each 10 cc. sample of heparinized blood is processed

† The fibrinogen is being prepared to meet the given specifications by the Pentex Corporation, Kankakee, Illinois. If this preparation meets specifications, the adjustments under "Preparation of Stock Fibrinogen Solution" will already have been made.

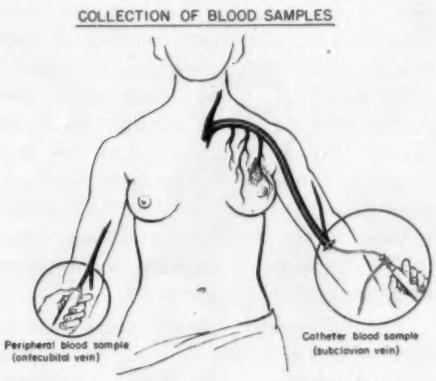


Fig. 1.—Collection of blood samples from the subclavian vein through a catheter and from the antecubital vein simultaneously.

immediately. Samples are obtained from one or all of three venous sources: (1) peripheral blood samples from antecubital venipuncture (Fig. 1); (2) aspiration of blood from a catheter inserted into the major venous trunk draining the tumor area (Fig. 1); (3) direct needle aspiration of blood from a vein draining the tumor site (Fig. 2).

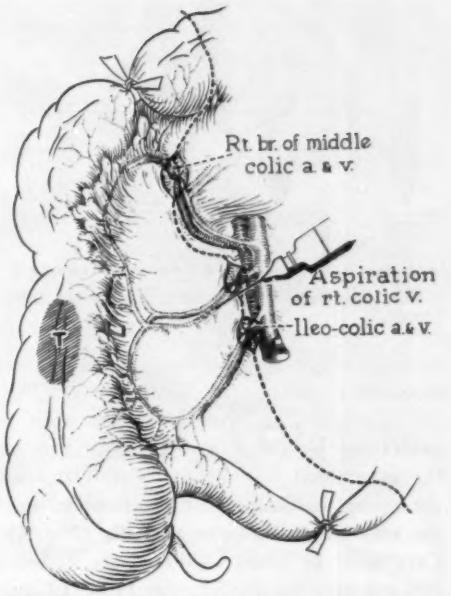
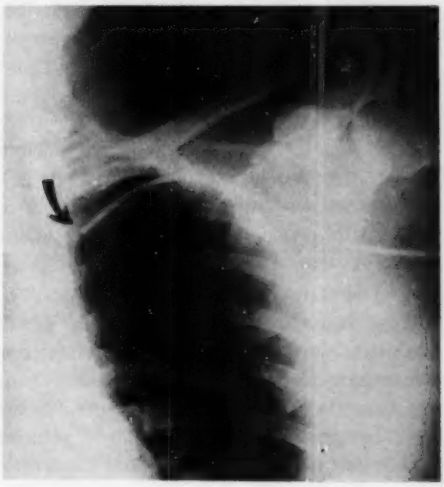


Fig. 2.—Collection of blood sample from a vein draining the tumor site (*T*) by direct needle aspiration. Modified from Cole et al.[7]

Catheterization of the inferior vena cava is carried out by a cut-down on the saphenofemoral junction, placing a No. 6 or No. 7 cardiac catheter in the long saphenous vein or one of its major branches under x-ray

Fig. 3.—X-ray showing catheter in the inferior vena cava of a patient about to undergo nephrectomy for carcinoma of the kidney. The tip of the catheter (arrow) is placed at the level of T-12 to L-1 in order to be above the renal veins.

Fig. 4.—X-ray showing catheter in the subclavian vein of a patient about to undergo radical mastectomy.



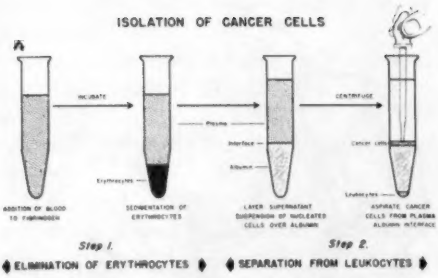


Fig. 5.—Isolation of cancer cells from whole blood.

or fluoroscopic control; the catheter is then threaded upward to the desired level (Fig. 3). Catheterization of subclavian vein is performed by either a direct cut-down on the antecubital vein or the introduction of the cardiac catheter into the antecubital vein via a thin-walled 14-gauge needle (Fig. 4). Care must be taken to thread the catheter upward into the basilic vein (Fig. 1) and thence to the subclavian vein, and not into the cephalic vein, where the catheter becomes arrested at the cephalic-axillary junction.

Coagulation of blood in the catheter is prevented by maintaining a constant drip of 500 cc. of 5% dextrose, to which 10 mg. of heparin has been added. Blood samples are obtained simultaneously from the catheter and the peripheral sites.

Isolation of Cancer Cells.—It should be emphasized that the method herein described is physiologic: No organic acids or saponin is used, and all materials (albumin and fibrinogen) are within the physiologic ranges of pH and osmolarity.

The isolation of cancer cells from whole blood is a two-step procedure: Step 1 is the elimination of erythrocytes; Step 2 is the separation of cancer cells from leukocytes, as seen in Figure 5.

The erythrocytes are first eliminated by the addition of fibrinogen, which causes rouleaux formation of erythrocytes and hence their accelerated sedimentation. Using the formula of Buckley et al.,[20] the number of cubic centimeters of fibrinogen solution and saline necessary for a final concentration of 6.7 mg. of fibrinogen per cubic centimeter at a hematocrit of 27% is determined. This fibrinogen-saline mixture is added to a 10 cc. blood sample, mixed thoroughly, and allowed to stand at room temperature for 20-45 minutes. In this short period of time the erythrocytes will sediment to within 80% to 85% of their packed volume, while the leukocytes and tumor cells will remain in the supernatant plasma in a homogeneous suspension.

The supernatant plasma suspension of cells is decanted and layered, maintaining a sharp interface, over 5 cc. of isosmotic albumin solution which has been adjusted to a specific gravity of 1.065, according to the formula of Agranoff et al.,[22] in a 15 cc. conical centrifuge tube. This specific gravity is intermediate between that of most adenocarcinoma cells and leukocytes.

The tube is then centrifuged at 1000 rpm for 10 minutes, or until the plasma is clear. The gravitational field must be applied slowly to avoid disrupting the interface. During centrifugation, as each cell reaches an interface of equal or higher specific gravity, the affected mass is reduced to zero, and the cell descent is arrested. Following centrifugation most of the leukocytes, which are heavier than the adjusted albumin, will be packed in the bottom of the centrifuge tube, while the majority of the tumor cells, which are lighter than the adjusted albumin, will be collected at the plasma-albumin interface. The tumor cells are then aspirated from the plasma-albumin interface by means of a Pasteur pipette, resuspended in 10 cc. of isotonic saline, and centrifuged for 10 minutes at 1000 rpm. After centrifugation, the supernatant saline is decanted, and the sediment of tumor cells is aspirated in a glass pipette and streaked on glass slides. The slides, while still wet, are placed in ether-alcohol solution and later stained, using the Papanicolaou technique. The resuspension of the cells in saline and recentrifugation removes albumin, which causes an undesirable red precipitate with the Papanicolaou stain.

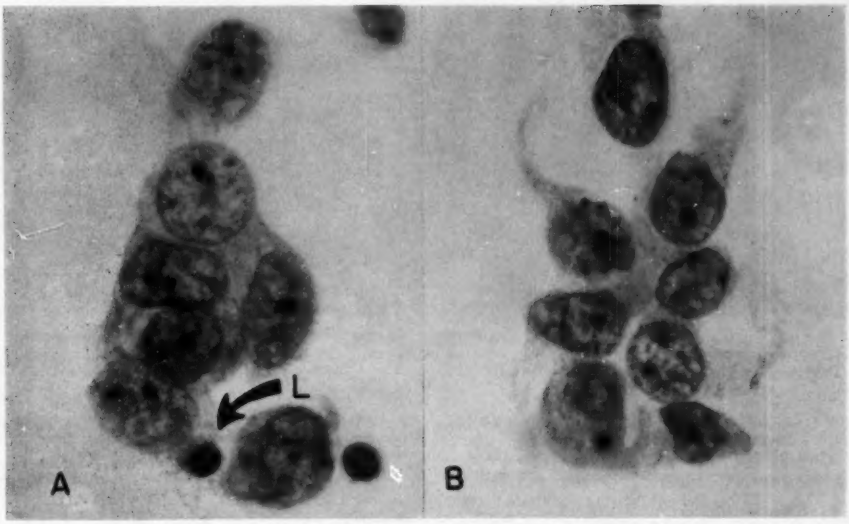


Fig. 6.—Cystadenocarcinoma of the ovary. *A*, clump of cancer cells isolated from the antecubital vein during surgery; *L*, lymphocyte. *B*, direct smear of resected tumor. Papanicolaou stain; × 1100.

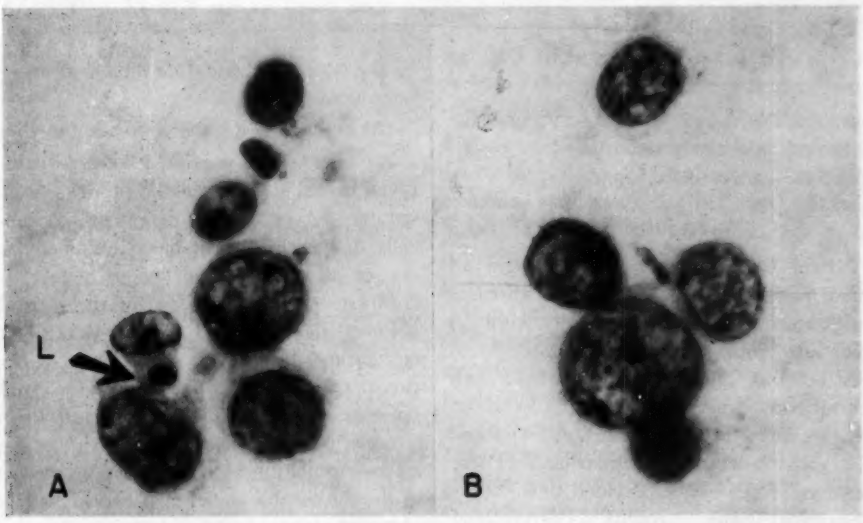


Fig. 7.—Carcinoma of the breast. *A*, group of cancer cells isolated from the antecubital vein during skin preparation prior to surgery; *L*, lymphocyte. *B*, direct smear of resected tumor. Papanicolaou stain; × 1100. Reproduced from article by W. H. Cole et al. (Bull. New York Acad. Med., to be published), by permission of the New York Academy of Medicine.

The remaining albumin is decanted from the original centrifuge tube, and the packed cells in the bottom are resuspended in saline, centrifuged, and streaked in a similar fashion. By this procedure none of the heavier tumor cells which may have passed through the plasma-albumin interface are lost.

Cytology.—In order to improve our accuracy of differentiation of tumor cells and normal blood cells, the cancer cells isolated by this technique are compared with a direct

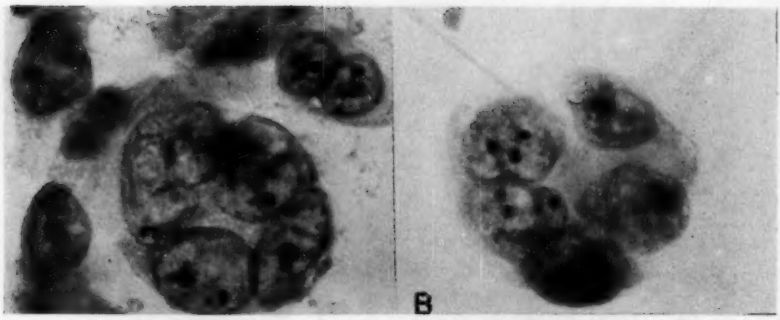


Fig. 8.—Cystadenocarcinoma of the ovary. *A*, clump of cancer cells forming an acinar structure from the antecubital vein during surgery. *B*, direct smear of resected tumor. Papanicolaou stain; × 1100.

TABLE 1.—*Summary of One Hundred Patients with Cancer (Blood Samples Obtained from Any or All of Three Venous Sources)*

	Curable Patients		Incurable Patients	
	Number	Positive	Number	Positive
Digestive tract	23	2	18	5
Genitourinary tract	11	4	3	1
Breast	23	4	2	2
Miscellaneous (ovary, lung, etc.)	15	2	5	1
	72	12 (16.7%)	28	9 (31.1%)

smear of the tumor (Figs. 6, 7, and 8). Cancer-cell counts are determined by counting all the cancer cells found.

Results

A total of 100 cancer patients and 14 control patients with nonmalignant diseases were studied. The cancer patients were divided into four groups: (1) those with digestive tract carcinomas; (2) those with genitourinary tract carcinomas, (3) those with carcinoma of the breast, and (4) those with miscellaneous malignancies. These groups were further subdivided into "curable" and "incurable" patients, as determined by the surgeon at the time the blood samples were obtained.

TABLE 2.—*Cancer of the Digestive Tract*

Site of Carcinoma	Curable Patients		Incurable Patients	
	Number	Positive	Number	Positive
Esophagus	0	0	3	0
Stomach	1	1	7	3
Colon	12	0	2	0
Rectum	10	1	2	0
Gallbladder	0	0	1	0
Pancreas	0	0	3	2
Total	23	2	18	5

TABLE 3.—*Cancer of the Genitourinary Tract*

	Curable Patients		Incurable Patients*	
	Number	Positive	Number	Positive
Ca kidney	3	0	2	1
Wilms tumor	2	2	0	0
Ca bladder	2	1	1	0
Ca prostate	3	1	0	0
Ca urethra	1	0	0	0
Total	11	4	3	1

Occurrence of Cancer Cells in the Blood.

A summary of the 100 cancer patients is given in Table 1. Of the 72 patients deemed curable, 12, or 16.7%, demonstrated cancer cells in the circulating blood obtained from one or all of the three venous sources. In contrast, 9 or 28, or 31%, of the incurable patients demonstrated cancer cells in the circulating blood. In the digestive tract carcinomas, 2 of 23, or 8.6%, of the curable patients and 5 of 18, or 27.8%, of the incurable patients demonstrated cancer cells in the circulating blood; the 2 positive cases in the 23 curable patients occurred in blood obtained from a vein draining from the

TABLE 4.—*Cancer of the Breast*

	Curable Patients		Incurable Patients	
	Number	Positive	Number	Positive
Radical	15	3	0	0
Simple	3	1	0	0
Recurrent (local)	4	0	0	0
Metastases	0	0	2	2
Paget's disease	1	0	0	0
Total	23	4	2	2

TABLE 5.—*Miscellaneous Cancers*

	Curable Patients		Incurable Patients	
	Number	Positive	Number	Positive
Ca ovary	3	2	0	0
Ca cervix	1	0	0	0
Ca tongue	1	0	0	0
Ca tonsil	1	0	0	0
Ca lung	3	0	1	0
Ca thyroid	2	0	0	0
Melanoma	2	0	2	1
Sarcoma	2	0	2	0
Total	15	2	5	1

tumor site, since peripheral blood was negative in all of the 23 cases tested. In the genitourinary tract carcinomas, 4 of 11, or 36.7%, of the curable and 1 of 3 of the incurable patients exhibited cancer cells in the circulating blood. In the group of carcinomas of the breast 4 of 23, or 17.4%, of the curable patients and 2 of 2 of the incurable patients demonstrated cancer cells in the circulating blood. Finally, in the miscellaneous group of carcinomas, 2 of 15, or 13.3%, of the curable patients and 1 of 5 of the incurable patients exhibited cancer cells in the circulating blood. A further breakdown of the various groups in Table 1 is given in Tables 2, 3, 4, and 5.

TABLE 6.—*Benign Disease: Summary of Control Patients* *

	No.	Positive
Fibroadenoma of breast	2	0
Polyp of colon	1	0
Polyp of bladder	1	0
Cyst of kidney	1	0
Cyst of gallbladder	1	0
Ulcer of stomach	3	0
Thyroid nodule	1	0
Fibrosis of vulva	1	0
Ulcerative colitis	1	0
Hemangioma	1	0
Leiomyoma of stomach	1	0
Total	14	0

* Malignancy was strongly considered in the differential diagnosis.

Table 6 summarizes the data for the 14 control patients, none of whom demonstrated cancer cells in the circulating blood. In these patients, malignancy was strongly considered in the differential diagnoses, but detailed examination was negative for malignancy.

Source of Positive Blood Samples.—Of 66 curable patients, 7, or 10.6%, exhibited cancer cells in the peripheral blood, while 4 of 11, or 36.4%, and 3 of 16, or 18.8%, of the curable patients demonstrated cancer cells in blood obtained by catheter and from the tumor site, respectively (Table 7). Cancer cells were found in the peripheral blood of 8 of 26, or 30.8%, of incurable patients.

In 22 cases of curable digestive tract cancer, cancer cells were not shown in the peripheral blood, while in 5 of 17, or 29.4%, of the cases of incurable digestive tract carcinoma cancer cells were demonstrated in the peripheral blood. These five cases included three carcinomas of the stomach and two carcinomas of the pancreas.

Role of Operative Manipulation.—Sixty-two patients were studied during an operative procedure. Of these, 12, or 19.3%, exhibited cancer cells in the circulating blood from any or all of three venous sources. Table 8 gives an analysis of these positive cases. Five cases were negative before manipulation and became positive with manipulation. These included two carcinomas of the breast, a carcinoma of the bladder, one carcinoma of the ovary (Fig. 9), and one carcinoma of the stomach, the last being the only incurable cancer. One patient, with carcinoma of the kidney, demonstrated cancer cells in the inferior vena

TABLE 7.—*Analysis of Source of Positive Blood Samples* *

	Curable Patients			Incurable Patients		
	Periph.	Cath.	Tumor Site	Periph.	Cath.	Tumor Site
Digestive tract	0 (22)	0 (0)	2 (9)	5 (17)	0 (1)	1 (2)
Genitourinary tract	2 (8)	2 (5)	1 (1)	0 (2)	1 (1)	0 (0)
Breast	3 (22)	2 (5)	0 (4)	2 (2)	0 (0)	0 (0)
Miscellaneous (ovary, lung, etc.)	2 (14)	0 (1)	0 (2)	1 (5)	0 (0)	0 (0)
Total	7 (66) or 10.6%	4 (11) or 36.4%	3 (16) or 18.8%	8 (26) or 30.8%	1 (2)	1 (2)

* Numbers in parentheses indicate total number in category.

TABLE 8.—*Analysis of Positive Cases During Surgery*

Negative before operation, but becoming positive with operative manipulation	5
Positive before operation, but showing increase with operative manipulation	1
Positive before operation, showing no increase with operative manipulation	1
Could not be evaluated (inadequate data)	5
Total	12

cava preoperatively, and showed a fourteenfold increase in the number of cancer cells upon manipulation, as illustrated in Figure 10. Another patient with carcinoma of the breast showed cancer cells in the circulating blood preoperatively, with no significant increase incident to the surgical manipulation, as shown in Figure 11. The role of operative manipulation could not be evaluated in the remaining five cases; two of these were cases of Wilms' tumor, in which only one sample was drawn during surgery, and three were cases of digestive tract carcinoma, in which peripheral blood samples were negative preoperatively and found to be positive by aspiration of blood from the tumor site during surgery. These cases included carcinoma of the rectum, stomach, and pancreas, only the last being incurable. Therefore, of the seven cases which had adequate data for the evaluation of the role of surgical manipulation, six showed a definite increase in cancer cells in the circulating blood.

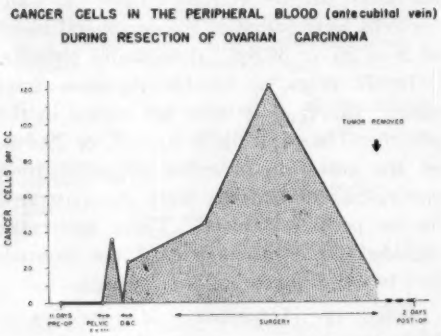

CANCER CELLS IN THE PERIPHERAL BLOOD (antecubital vein)
DURING RESECTION OF OVARIAN CARCINOMA
CANCER CELLS per C.C.
TUMOR REMOVED
SURGERY

Fig. 9.—Cancer cells in the antecubital vein during resection of ovarian carcinoma. The tumor, which was resectable, had invaded a portion of the uterine fundus. Reproduced from article by S. S. Roberts et al. (S. Forum, to be published) by permission of the American College of Surgeons, Chicago.

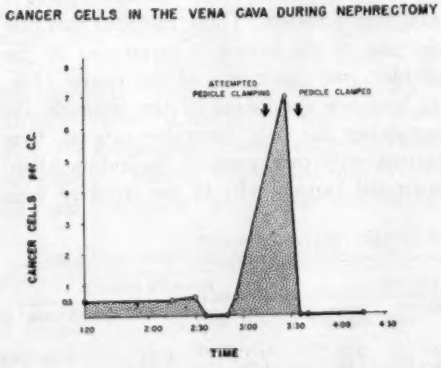


Fig. 10.—Cancer cells in the vena cava during nephrectomy for carcinoma of the kidney. This patient died six months postoperatively with x-ray evidence of massive pulmonary metastases. Reproduced from article by S. S. Roberts et al. (S. Forum, to be published) by permission of the American College of Surgeons, Chicago.

Comment

Collection of Blood Samples.—It was anticipated that the occurrence of cancer cells in the peripheral blood would be low, due to the factor of capillary filtration. Therefore, to short-circuit the capillary beds, and to lessen the factor of dilution and destruction of cancer cells by the host, techniques for obtaining blood samples from the veins draining the tumor site were utilized. Few

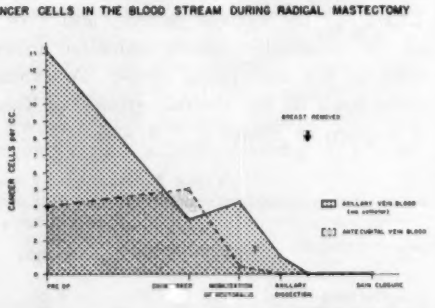


Fig. 11.—Cancer cells in the blood stream during radical mastectomy. Blood samples were drawn simultaneously from the axillary vein through a catheter and from the antecubital vein. Reproduced from article by S. S. Roberts et al. (S. Forum, to be published) by permission of the American College of Surgeons.

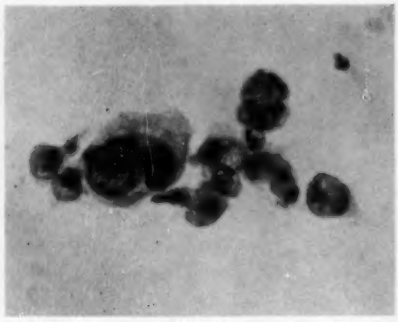


Fig. 12.—Carcinoma of the breast. Clump of cancer cells drawn from the axillary vein through a catheter during skin preparation prior to surgery. Papanicolaou stain; × 500.

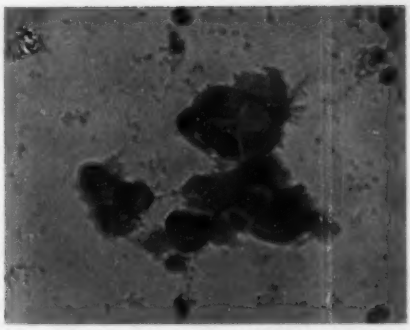


Fig. 13.—Carcinoma of the kidney. Clump of cancer cells drawn from the inferior vena cava through a catheter during surgery. Papanicolaou stain; × 500.

tumors other than gastrointestinal tract malignancies lend themselves well to the direct needle aspiration of blood from a collecting vein from the tumor site. Because of this, blood was aspirated from a cardiac catheter positioned in the major venous trunk draining the tumor area (Figs. 3 and 4). In every positive case in which catheter and peripheral samples were obtained simultaneously, both were positive. However, in general, more cancer cells and larger clumps were found in the catheter samples (Figs. 12 and 13).

Method.—The method was chosen to maintain the maximum cellular detail and staining qualities for cytologic studies and for the preservation of viable cells for in vivo studies. The saponin or the glacial acetic acid used in hemolytic techniques alters the staining qualities and kills the cells. This method is not quantitative because many of the heavier cancer cells, notably squamous-cell types, sediment with the erythrocytes after the addition of fibrinogen. However, the identical processing of each sample allows for comparison within that case.

Cytologic examination of the nucleated cells obtained from Step 1 (Fig. 5) revealed so many leukocytes, as compared with cancer cells, that the additional separation of cancer cells was necessary for easier identification. Accordingly, the albumin-flotation method of Step 2 was utilized.

Cytology.—Prior to the epochal work of Papanicalaou in establishing the science of exfoliative cytology, definite identification of the "abnormal" cells in the blood stream was controversial; however, with this stain,

Fig. 14.—Carcinoma of the kidney. Cancer cell drawn from the inferior vena cava through a catheter during surgery. Papanicolaou stain; × 1100.

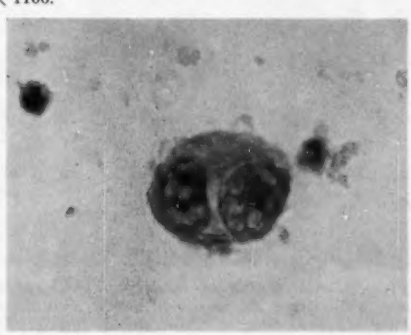
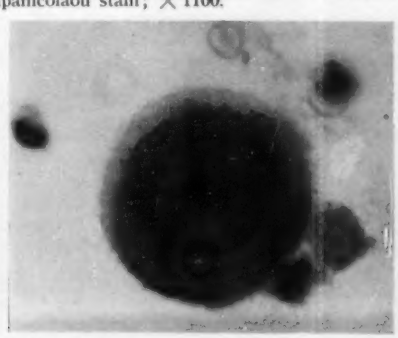


Fig. 15.—Malignant melanoma. Cancer cell from the antecubital vein of an incurable patient. Papanicolaou stain; × 1100.



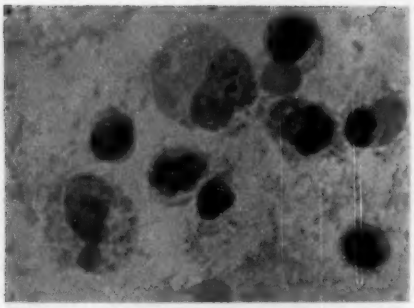


Fig. 16.—Wilms' tumor. Cancer cells drawn from the inferior vena through a catheter during skin preparation prior to surgery. Papanicolaou stain; × 1100.

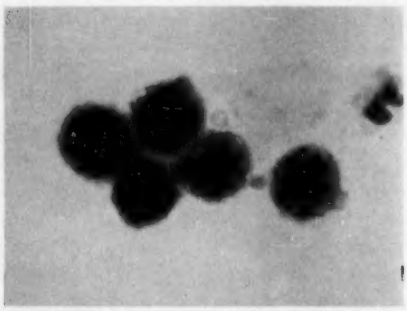
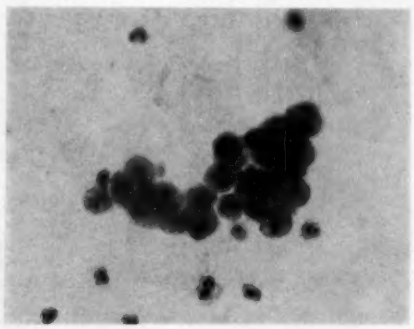


Fig. 17.—Carcinoma of the stomach. Group of cancer cells from the antecubital vein prior to operation. Papanicolaou stain; × 1100.

single-cell identification of cancer cells in the circulating blood was possible. Although many single cancer cells were seen (Figs. 14, 15, and 16), the majority of the positive cases exhibited clumps of cancer cells (Figs. 6, 7, 8, 12, 13, 17, 18, and 19). The cells identified as cancer cells were identical with those obtained by direct tumor smear (Figs. 6, 7, and 8) and were confirmed by one of us (E. A. M.), a professional cytologist.

Occurrence of Cancer Cells in the Circulating Blood.—The finding of cancer cells in the peripheral blood of 10.6% of curable patients is comparable to that of Engell,[6] who reported cells in 12.6% of curable patients in a similar series. Engell found cancer cells in the peripheral blood of 50% of incurable cases, as compared with our result of 30.8% for incurable cases; however, the cases included in our series were not as advanced as Engell's. There appears to be a direct relationship between the advancing stage of the disease and the percentage of positive blood samples. No cancer cells were found in the circulating blood of patients with very early carcinomas. Accordingly, this technique would be of limited value as a screening procedure. In carcinomas of the digestive tract, no cells were found in the peripheral blood until the case had advanced to an incurable status locally. This may represent a direct action of the liver on the filtration of malignant cells from the venous blood of the portal system. It is possible that the occurrence of cancer cells in the peripheral blood of a patient with a gastrointestinal carcinoma may indicate a dire prognosis. The finding of cancer cells in the peripheral blood, even in large clumps of 65 cells, demonstrates that they have traversed the

Fig. 18.—Carcinoma of the stomach. Clump of cancer cells from the antecubital vein prior to operation. Papanicolaou stain; × 500.



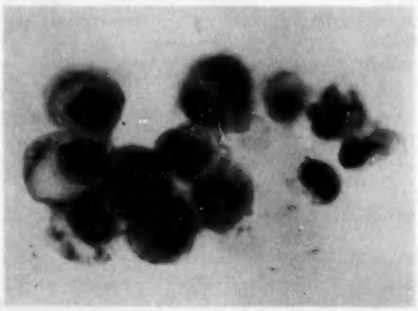


Fig. 19.—Carcinoma of the rectum. Clump of cancer cells from the superior hemorrhoidal vein during surgery. Papanicolaou stain; × 1100.

vascular channels of the lungs and peripheral vessels. This gives rise to speculation as to the nature of this passage, whether by arteriovenous shunts as demonstrated by Zeidman and Buss,[25] by ameboid movement, or by changes in caliber of the minute vessels in the capillary beds with the passage of formed elements, as demonstrated by Converse and Rapaport.[26] The highest percentage of positive cases for curable patients was found in the carcinomas of the genitourinary tract, in which blood vessel invasion is so often seen.

Although sex differences have been noted for specific cancer,[27] evaluation of the occurrence of cancer cells in the circulating blood for the 100 cancer patients gave no significant difference with regard to sex.

Role of Surgical Manipulation.—The renewed interest in the vascular spread of cancer by Cole et al.,[7] Fisher and Turnbull,[14] and Engell [6] makes the evaluation of the role of surgical manipulation of paramount importance. Early investigation by Jonescu [28] and Ide et al.[29] indicated a relationship experimentally. Engell [6] found no relation to surgical manipulation. The finding of an increase in the incidence of cancer cells in the circulating blood in six of seven cases in our series (Table 8), along with the graphic demonstration of the increase with actual manipulation (Figs. 9 and 10), leads us to conclude that there is a direct relation between the manipulation incident to surgery and the number of cancer cells in the circulating blood. The case illustrated in Figure 9 is that of a patient with an ovarian carcinoma. A shower of cancer cells in the peripheral blood was shown following a pelvic examination under anesthesia, during which the cystadenocarcinoma was accidentally ruptured, with a secondary rise occurring subsequent to dilatation and curettage. The number of cells continued to increase with the surgical procedure. Figure 10 illustrates a patient with renal-cell carcinoma who demonstrated a shower of cancer cells incident to the vigorous manipulation associated with the application of the pedicle clamp. In contrast, a patient with carcinoma of the breast (Fig. 11) exhibited more cells preoperatively than at any time during the surgical procedure. In the patient with carcinoma of the breast and the patient with carcinoma of the kidney, no cancer cells were found in the circulating blood within minutes after the removal of the primary tumor. Confirmation of the direct relationship between manipulation and the number of cancer cells in the circulating blood is available from data obtained by Moore et al.[30] and Turnbull.[31]

Summary and Conclusions

A method for the isolation of cancer cells from blood utilizing differences in specific gravities is described. In a study of 100 cancer patients, cancer cells have been demonstrated in the circulating blood (from any or all of three venous sources) in 16.7% of curable and in 31.1% of incurable patients, indicating that there is apparently a direct relationship between the advancing stage of the disease and the percentage of positive blood samples. In six of the seven positive cases with adequate data studied before and during surgery, there appears to be an increase in the number of cancer cells in the circulating blood during manipulation incident to resection of the tumor. In two carefully studied cases the cancer cells disappeared from the circulating blood within minutes following removal of the primary carcinoma.

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REFERENCES

1. Brown, C. E., and Warren, S.: Visceral Metastasis from Rectal Carcinoma, Surg. Gynec. & Obst. 66:611, 1938.

2. Dukes, C. W., and Bussey, H. J. R.: Venous Spread in Rectal Cancer, Proc. Roy. Soc. Med. 34:571, 1941.

3. Dukes, C. W.: Surgical Pathology of Rectal Cancer, Proc. Roy. Soc. Med. 37:131, 1944.

4. Grinnell, R. S.: The Spread of Carcinoma of the Colon and Rectum, Cancer 3:641, 1950.

5. Pool, E. H., and Dunlop, G. R.: Cancer Cells in the Blood Stream, Am. J. Cancer 21:99, 1934.

6. Engell, H. C.: Cancer Cells in the Circulating Blood, Acta chir. scandinav. supp. 201, 1955.

7. Cole, W. H.; Packard, D., and Southwick, H. W.: Carcinoma of the Colon with Special Reference to Prevention of Recurrence, J. A. M. A. 155:1549, 1954.

8. Ashworth, T. R.: A Case of Cancer in Which Cells Similar to Those in the Tumours Were Seen in the Blood After Death, Australian M. J. 14:146, 1869.

9. Schleip, K.: Zur Diagnose von Knochenmarkstumoren aus dem Blutbefunde, Ztschr. klin. Med. 59:261, 1906.

10. Aschoff, L.: Ein Fall von Myelom, München. med. Wchnschr. 53:337, 1906.

11. Ward, G. R.: The Blood in Cancer with Bone Metastases, Lancet 1:676, 1913.

12. Marcus, H.: Krebszellen im strömenden Blut? Ztschr. Krebsforsch. 16:217, 1917.

13. Quensel, U.: Zur Kenntnis des Vorkommens von Geschwulstzellen im zirkulierenden Blute, Upsala läkaref. förh. 26:1, 1921.

14. Fisher, E. R., and Turnbull, R. B., Jr.: The Cytologic Demonstration and Significance of Tumor Cells in the Mesenteric Venous Blood in Patients with Colorectal Carcinoma, Surg. Gynec. & Obst. 100:102, 1955.

15. Moore, G. E.; Sandberg, A., and Schubarg, J. R.: Clinical and Experimental Observations of the Occurrence and Fate of Tumor Cells in the Blood Stream, Ann. Surg. 146:580, 1957.

16. Ferrebee, J. W., and Geiman, Q. M.: Studies on Malarial Parasites: III. A Procedure for Preparing Concentrates of Plasmodium Vivax, J. Infect. Dis. 78:173, 1946.

17. Vallee, B. L.; Hughes, W. L., Jr., and Gibson, J. G., II: A Method for Separation of Leukocytes from Whole Blood by Flotation on Serum Albumin, Blood, Special Issue, No. 1, p. 82, 1947.

18. Fawcett, D. W.; Vallee, B. L., and Soule, M. H.: A Method of Concentration and Segregation of Malignant Cells from Bloody, Pleural, and Peritoneal Fluids, Science 111:34, 1950.

19. McGrew, E. A.: Concentration of Cells from Body Fluids for Cytologic Study, Am. J. Clin. Path. 24:1025, 1954.

20. Buckley, E. S., Jr.; Powell, M. J., and Gibson, J. G., II: The Separation of the Formed Elements of Whole Blood by Fraction I, J. Lab. & Clin. Med. 36:29, 1950.

21. Li, J. G., and Osgood, E. E.: A Method for the Rapid Separation of Leukocytes and Nucleated Erythrocytes from Blood or Marrow with a Phytohemagglutinin from Red Beans (Phaseolus Vulgaris), Blood 4:670, 1949.

22. Agranoff, B. W.; Vallee, B. L., and Waugh, D. F.: Centrifugal Subfractionation of Polymorphonuclear Leukocytes, Lymphocytes, and Erythrocytes, Blood 9:804, 1954.

23. Cole, W. H.; Roberts, S.; Watne, A.; McDonald, G., and McGrew, E. A.: The Dissemination of Cancer Cells, Bull. New York Acad. Med., to be published.

24. Roberts, S. S.; Watne, A. L.; McGrew, E. A.; McGrath, R. G.; Nanos, S., and Cole, W. H.: Cancer Cells in the Circulating Blood, S. Forum, 1957, to be published.

25. Zeidman, I., and Buss, J. M.: Transpulmonary Passage of Tumor Cell Emboli, Cancer Res. 12:731, 1952.

26. Converse, J. M., and Rapaport, F. T.: The Vascularization of Skin Autografts and Homografts, Ann. Surg. 143:306, 1956.

27. Baird, W. F., and Fisher, E. R.: Sex Differences in the Spread of Colorectal and Vesicle Carcinomas, Ann. Surg. 143:284, 1956.

28. Jonescu, P.: Über das Vorkommen von Geschwulstzellen im strömenden Blut von Tieren mit Impftumoren, Ztschr. Krebsforsch. 33:264, 1930.

29. Ide, A. G.; Harvey, R. A., and Warren, S. L.: Rôle Played by Trauma in the Dissemination of Tumor Fragments by the Circulation; Tumor Studied: Brown-Pearce Rabbit Epithelioma, Arch. Path. 28:851, 1939.

30. Moore, G. E.; Katz, A. D.; Sandberg, A. A., and Burke, E. M.: Incidence of Tumor Cells in Blood and Peritoneal Fluid in Patients with Cancer, S. Forum, to be published.

31. Turnbull, R. B., Jr.: Personal communication to the author.

Subarachnoid Alcohol Block in the Management of Pain of Malignant Disease

D. M. PERESE, M.D., Buffalo

Subarachnoid alcohol block is a method meriting the attention of every physician who wishes to control the pain in patients with malignant disease.

In the 1930's, initial reports describing the technique and indications for the procedure were made by Dogliotti,[8] Abraham,[2] Pitts,[27] Groff,[15] Owings,[24] Saltzstein,[31] and Stern.[32,33] At the same time, papers by Olmsted [22] and Labat [18] outlined the mechanism of the action of the alcohol on the nerves.

However, serious complications resulted from the use of subarachnoid alcohol block,[4,6,11,23,26,36] and it was difficult to obtain analgesia for longer than six weeks. Therefore, after this period, neurosurgical measures (rhizotomy, tractotomy, lobotomy, etc.) were used to a greater extent than previously to control pain caused by malignant lesions. Table 1 summarizes the significant publications dealing with alcohol block over the past 20 years.

Recently the literature has reflected a new trend, a return to the chemical rhizotomy using absolute alcohol.[5] Phenol [19] and ammonium sulfate [17] have also been tried for this purpose.

By presenting their advantages over neurosurgical measures, Bonica [5] spearheaded the drive for wider application of the various alcohol blocks in the management of pain caused by malignant disease. He showed that neurosurgical measures carried a greater risk than alcohol block by comparing his results with those of early neurosurgical publications.[12,22] However, such a risk may be worth while in the face of prolonged suffering, for several months or years, from pain which is not satisfactorily controlled by subarachnoid block alone.

Because of improved neurosurgical technique and better pre- and postoperative care, the risk of neurosurgical intervention has been lowered in the past 10 years.[25,38] Indications for tractotomy remain the same—that is, the need to control pain longer than the relief obtained from subarachnoid blocks, and with greater efficacy. But the advantages of alcohol block, in well-selected patients, still make it an important tool for the physician with special training in nerve blocks. The complications resulting from the use of al-

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TABLE 1.—*Early Results of Subarachnoid Alcohol Block*

Author	No. of Patients	Blocks	Amount Injected, Cc.	Complete Relief, %	Duration	Partial Relief, %	Duration	Slight or No Relief, %	Complications, %
Abbott[1]	25	40	0.75–1	84	1 mo. and longer	8	5 mo. and longer	8	4
Adson[9]	40	43	0.4–0.5	40	--	30	--	30	13
Dunphy & Alt[9]	13	18	0.8–2	46	9 mo.	39	6 mo.	15	61
Greenhill & Schmitz[14]	40	--	0.5–0.75	85	18 mo.	5	9 mo.	10	24
Harney & Kehres[16]	10	34	0.5–4	70	3 mo. and longer	30	Permanent	0	7
Poppen[25]	82	116	1	68	--	18	--	14	--
Russell[28]	22	29	0.4–1.5	64	2 yr.	27	2 mo.	9	65
Saltzstein[31]	11	12	0.35–1	91	5 mo.	9	36 hr.	0	64
Stern[33]	19	26	0.5–1	68	1–8 mo.	32	6 wk.-4 mo.	0	5
Truelson[35]	69	150	0.5–1.5	59	1 mo. and longer	23	1 mo.	18	20
White[37]	6	7	1–1.2	83	11 mo.	17	1 mo.	0	17

cohol can be lowered by following certain precautions, to be discussed later.

Rationale of Therapy for Pain of Malignant Disease

Contrary to general belief, the pain of malignant disease is rarely as severe as the pain of some benign conditions, such as kidney colic, severe gallbladder attack, severe migraine, etc. It is the continuous, unrelenting quality of the pain, supplemented by fear of the unknown, that wears down the patient's mental and physical reserves. Consequently, life affords the patient little enjoyment, and he ceases to be socially useful.

Interrupting the pain impulses reaching the level of consciousness is the most important step in treating pain of chronic nature. However, psychotherapy and tranquilizing drugs are of great value in alleviating the patient's fears and relieving his anxiety.

Alcohol, when introduced into the subarachnoid space, produces a chemical rhizotomy by destroying the nerve fibers with which it comes in contact. To be effective, in doses which can be employed with safety, alcohol must be deposited in the nerve substance or within a few millimeters of the nerve. In blocking the sympathetic ganglia, the relatively large size of the nervous network makes it an easier target than a single peripheral nerve.[34]

Since Dargent[7] demonstrated the role of the sympathetic ganglia in producing the pain of cancer, other agents, such as phenol, have been tried, with better results than alcohol, in blocking the sympathetic ganglia.[20] However, when aqueous phenol was introduced into the subarachnoid space, some complications still occurred.[19] In general, 95% alcohol is preferred over other agents[5] because of widespread experience (Table 1) in its use and the consistency of its results when used properly. In my opinion, handling each case on its own merits remains the better method of treatment, rather than employing any one agent for all types of pain caused by malignant disease.[10,25]

Indications

I chose the patients for subarachnoid alcohol block among two groups: (1) patients with advanced disease whose condition would not tolerate radical surgical procedures, and (2) patients who were in good general condition and had pain of short duration (four to eight weeks of continuous pain), whose life expectancy was longer than one year, and to whom I did not wish to administer narcotics lest their mental faculties be impaired.

I have been able to duplicate the prolonged relief (one month or longer) obtained with subarachnoid alcohol block by Poppen[28] and Truelsen[35] without encountering many permanent complications.

My experience in treating patients suffering from pain of malignancy with subarachnoid alcohol block will form the basis of this paper.

Material

Over a three-year period, 70 patients were treated. Histologic identification of their malignant lesions was as follows: carcinoma of the cervix, uterus, and vagina, 22; carcinoma of the rectum and colon, 13; carcinoma of the breast, 9; carcinoma of the lung, 6; malignant lymphoma, 3; carcinoma of undetermined origin, 3; malignancies of miscellaneous origin, 14.

The duration of pain before the block was short (from two to six weeks) in only 15 patients. Most of them had suffered from their pain longer: 12 patients from 1½ to 3 months; 21 patients from 4 to 6 months, and 22 patients from 6 to 18 months. All patients had been treated with palliative x-irradiation, surgical intervention, hormones, chemotherapeutic agents, etc., before they were referred to the neurosurgery department for relief of their suffering.

These 70 patients had a total of 119 subarachnoid alcohol blocks. Sixty-two patients had one or two blocks; five patients, three or four blocks, and three patients, five blocks. Four to seven days elapsed before a subsequent block was attempted. One reason for administering more than one block is the bilaterality of the pain. When pain persisted four to seven days after the block, a repetition was considered. Another reason for repeating the block in the same region is failure of the preceding one. The patient was checked for residual urine, sensory changes, and motor weakness,

and if there was no neurologic deficit, another block was done.

Method

Every patient, on admission, received a complete neurologic evaluation and check for residual urine before the injection. An existing neurologic deficit did not necessarily contraindicate the procedure. By knowing the exact status of each patient before the block, my associates and I could evaluate the results of the procedure accurately. However, I consider the following situations as contraindications:

1. Tumor in the extradural, subdural, or subarachnoid space demonstrated by neurologic examination and roentgenography or myelography. In patients who have metastatic tumors in the extradural space and who have severe pain, surgical decompression is advisable to relieve the pressure if their general condition permits. This therapy should be supplemented by x-irradiation and chemotherapy when indicated before resorting to an alcohol block.

2. The appearance of serious neurologic deficits (relaxation of sphincter tone, weakness, etc.). These difficulties preclude the administration of another alcohol block before they clear up, even though the pain is not relieved. A repeat block under these circumstances gives no assurance of alleviating the pain, and chances of serious permanent complications are definitely increased. After two weeks the patient is reevaluated. If the neurologic deficit has not improved, another alcohol block is not performed. Depending upon his physical status, the patient is either placed (or continued) on narcotics, or a tractotomy is advised, especially when his life expectancy is two months or longer.

Until Bonica's[5] paper and this report, almost all authors were performing alcohol blocks in the lumbar region. The distribution of the level of my blocks was as follows: cervical region, 16; upper thoracic region, 7; lower thoracic region, 36; thoracolumbar region, 49, and lumbar region, 11 (Table 2).

Technique

The following paragraphs outline the important aspects of my technique:

TABLE 2.—*Location of Blocks*

Cervical	16
Thoracic	
(*a*) T-1 to T-6	7
(*b*) T-7 to T-12	36
Thoracolumbar	
(*a*) T-11 to T-12 and T-12 to L-1	34
(*b*) T-12 to L-1 and L-1 to L-2	15
Lumbar	11
	119

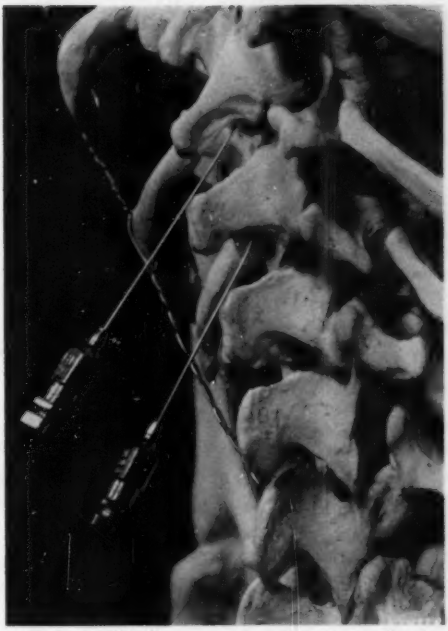
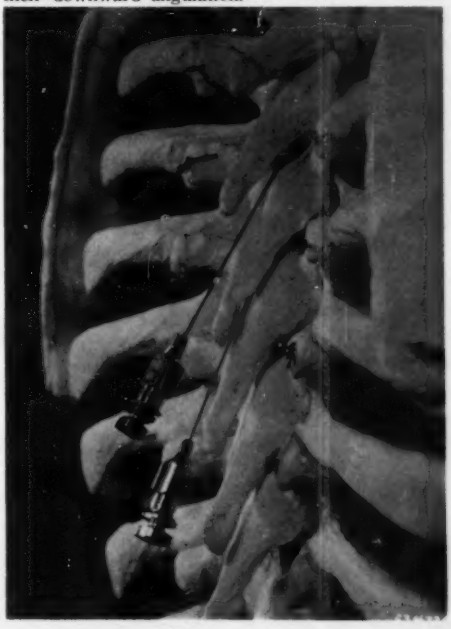


Fig. 1.—Needles are in the thoracolumbar region. The uppermost needle is at the T-11 and T-12 interspace; the lowermost needle is at the T-12 and L-1 interspace.

Fig. 2.—Needles are at the T-4 and T-5 and at the T-5 and T-6 interspaces. Note the fish-scale arrangement of the spinous processes and their downward angulation.



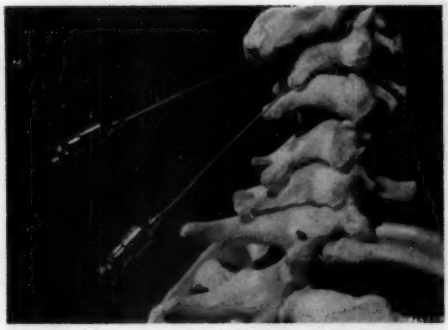


Fig. 3.—Needles are at the C-2 and C-3 and at the C-3 and C-4 interspace. The bifid spine of the second cervical vertebra is easily palpable through the skin under the foramen magnum. (C-1 has no spinous process.)

Fig. 4.—Anterior tilting of the body is accomplished after the introduction of the spinal needles.

1. A No. 22 spinal needle is used. A short-beveled needle is preferred over regular needles for introduction between T-9 and L-2 (Fig. 1), where the distance between the dura and the spinal cord is not great (2 to 3 mm.). A regular-beveled needle is used between T-2 and T-9 (Fig. 2), where the angle of the spinous processes is oblique and the distance between the spinal cord and the dura is relatively long (3 to 4 mm.). In all cervical areas, a short-beveled needle is used because of the likelihood of starting bleeding where the blood vessels are large and easily injured. Although the dura is quite thick in this region, a short-beveled needle goes through with ease (Fig. 3).

2. The level of injection should correspond to the actual dermatome of pain; that is, the tip of one needle should be at the level of the entrance to the spinal cord of the sensory root affected by the pain. Therefore, one needle is placed in the interspace corresponding to the level of pain and another needle one or two levels above. Thus, when the alcohol is injected, it will also bathe the adjacent sensory nerve roots. It is necessary to elevate the point of injection and tilt the body forward 45 degrees just before injecting the alcohol (Fig. 4). A total of 1.0 cc. of 95% alcohol is divided equally between two needles, that is, 0.5 cc. to each. The entire amount is injected during a two-minute period (Fig. 5).

3. The introduction of the needle requires special care and gentleness, so that as the needle advances one is aware of each structure that it perforates. The habit of advancing the needle for an estimated distance and then pulling out the stylet to see if there is

Fig. 5.—Note the position of the fingers, which are bracing the hub of the needle during the injection of alcohol.

Fig. 6.—Needles are in the L-3 and L-4 and in the L-4 and L-5 interspaces. The opening of the spinous processes is achieved by anterior flexion of the spine.

cerebrospinal fluid is not recommended. Usually one feels when the dura is entered. Because of the small bore of the needle, one has to wait 10 to 30 seconds before replacing the stylet and advancing it farther. When the needle has completely entered the subarachnoid space, the flow of the cerebrospinal fluid is quite slow in the absence of elevated pressure.

Difficulties will arise during the advancement of the needle (*a*) if the needle is not precisely in the midline, (*b*) if the direction of advancement is not parallel to the spinous processes at the corresponding levels (one should study a skeleton or Figures 1, 2, 3, and 6), (*c*) if the groove along the undersurface of the upper thoracic spines is not followed as a guiding channel for the needle, or (*d*) if the advancement of the needle is sudden and rapid. (One can easily pierce the cord and reach the undersurface of it near the body of the vertebra and still obtain cerebrospinal fluid, although this is usually blood-tinged. If so, no alcohol should be injected before complete assessment of the neurologic status of the patient. Usually it is better to postpone the procedure for at least a week to evaluate the patient.)

If one does not follow those precautions, the needle will hit either the laminal arch of the vertebra or its body after going through the cord. This happened several times in my experience. The patient suffered no neurologic deficit but complained of sharp pain. In one instance, alcohol was injected despite the appearance of bloody cerebrospinal fluid, and the patient developed complete foot drop and weakness of the leg. This was our only serious complication in 119 alcohol blocks.

4. The position of the patient is very important. The needle can be introduced with the patient in either a sitting or a side position. Before injection the patient is placed on his side, leaning anteriorly 45 degrees (Fig. 4), so that the posterior nerve roots, as they enter the cord, will be uppermost. In this way, only the nerve roots to be blocked will absorb the rising alcohol in the spinal fluid. This position is achieved either by using pillows under the flanks or by lowering or elevating the head of the table 5 to 10 degrees (Fig. 7).

Fig. 7.—The head of the operating table is lowered 10 degrees in order to allow the alcohol to bathe the nerve roots near the needles, which are in the lower thoracic area.

5. During the injection the patient should complain of a burning sensation along the dermatomes affected. If the burning pain is not exactly along the desired region, it is better to stop the injection, rather than continue, then evaluate the whole situation, and adjust the needle if necessary.

6. After the injection is completed, the patient is left in the same position without moving his legs or arms for 30 to 45 minutes. Premedication of the patient with morphine and scopolamine is helpful in keeping him comfortable during the procedure.

7. Postoperatively, the patient is kept in bed for 24 to 48 hours and checked for residual urine, weakness, and sensory changes.

The efficacy of the block cannot be evaluated satisfactorily for at least three or four days after the alcohol block, for it takes several days to overcome the acute irritations of the procedure (such as headache, pain at the point of injection, etc.). At the end of a week one can definitely tell whether this operation should be repeated or not.

Results

Bonica [5] published one of the most recent series of subarachnoid alcohol blocks in the management of pain from malignant dis-

TABLE 3.—*Recent Results of Subarachnoid Alcohol Block*

Authors	No. of Patients	Relief			Complications (Paresis, Weakness Incontinence)
		Complete	Partial	Slight or None	
Bonica[4]	70	38 (54%)	24 (34%)	8 (12%)	25 (36%)
Perese	70	41 (59%)	26 (37%)	3 (4%)	10 (14%)

ease. He treated 194 patients using various types of blocks. Seventy patients had subarachnoid injection of alcohol. Of these, 38 patients obtained complete relief; 24, partial relief, and 8, slight or no relief. The corresponding figures in my series are 41, 26 and 3, respectively (Table 3). Bonica's technique differed from mine; he inserted more than two needles each time (usually four or five) and injected between 0.4 and 0.5 cc. of alcohol through each needle. Despite the increased amount of total alcohol injected in one sitting, his results did not improve over those of other authors using a maximum of 1 or 2 cc. in one sitting (Table 1). However, his incidence of complications was greater. Serious complications, consisting of paresis, weakness of extremities, and loss of sphincter control, occurred in 25 of his 70 patients. Although some of them recovered the lost functions after a period varying from five weeks to three months, others did not.

In my experience, serious complications occurred in 10 patients. Two patients developed weakness of one leg after the third series of alcohol injection. One of them was unable to use that leg in walking for a week (the needle had pierced his cord). He improved slowly, and 80% of his strength had returned two months after the block. Both of these patients were able to walk without assistance. Seven patients had bladder and sphincter incontinence after alcohol block; all of them regained normal function after four weeks except one, who died of her disease two weeks after the block. Another patient developed diplopia because of weakness of the sixth nerve after the third alcohol block performed at the C-1 and C-2 level. This diplopia lasted two months.

TABLE 4.—*Duration of Relief*

Time	Complete	Partial
1–2 wk	7	8
2–4 wk	3	2
4–12 wk	8	3
12–26 wk	3	0
6 mo. or longer	20	12
	41	16

Less serious complications, such as emesis, headache, stiff neck, and paresthesias, were noted in 20 patients; all of them cleared within six weeks. Since Bonica does not give the number of less serious complications in his paper, a comparison cannot be made.

In evaluating the results of the subarachnoid alcohol block, one must consider the duration of relief, which is an important factor in the decision to undertake the injection rather than operative attack. The duration of relief from pain is tabulated in Table 4.

Almost all patients were relieved of their pain for longer than one month, some of them for longer than one year. In the group of patients who had partial relief, the recurrence of the initial pain was commoner than in those who had complete relief. When their pain was not satisfactorily controlled with subarachnoid alcohol block, the patients were treated with spinothalamic chordotomy, provided that their status permitted such an undertaking.

In the group of patients who obtained complete relief, only three required surgical intervention. There were two patients who had subarachnoid alcohol blocks three to six months after chordotomy because their initial pain returned. One of them, six weeks after the block, was still free of pain. Another patient died two months after the alcohol injection without any relief from pain.

The reasons for persistent midline pain and its management are outside the scope

of this paper. They will be discussed, along with spinal tractotomies, in another paper.

Summary

Subarachnoid alcohol block is a valuable tool in the management of pain in malignant disease. This procedure carries certain risks and must be undertaken by physicians trained in the performance of nerve blocks.

1. During a three-year period, 70 patients with malignancy of various types were treated with subarachnoid alcohol blocks. A total of 119 subarachnoid alcohol blocks was performed on 70 patients. One or two blocks were administered to 62 patients; three or four blocks, to 5 patients; five blocks, to 3 patients. The main reason for giving more than one block is the bilaterality of the pain.

The locations of the blocks were as follows: cervical region, 16; upper thoracic region, 7; lower thoracic region, 36; thoracolumbar region, 49, and lumbar region, 11.

2. Each patient was examined to determine the status of muscle strength in the legs and bladder function. Patients with pain of short duration, as well as those with pain of long duration, were treated with alcohol blocks after x-irradiation, hormones, etc., had failed to give them relief. Patients with short life expectancy (six to eight weeks) especially benefited from this procedure, since alcohol block would most likely provide relief for this length of time.

3. Of the 70 patients, 41 had complete relief of their pain, the duration varying from two weeks to a year or longer; 26 patients had partial relief, and 3 patients had slight or no relief. Almost all the patients who had partial or no relief lived long enough to develop additional pain because of advancing disease and were subjected to surgical methods of pain relief (chordotomy, etc.). Serious complications (paresis, weakness, or incontinence) occurred in 10 patients. Nine patients recovered within two months after the alcohol injection. The other patient died two weeks after the block because of progression of her disease.

Addendum

During the past 6 months, we have completed an additional 29 alcohol blocks on 25 patients with malignancy. Of these, 16 received complete relief, 6 had partial relief and 3 had no relief. No complications ensued.

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REFERENCES

1. Abbott, W. D.: Intraspinal Injection of Absolute Alcohol for Intractable Pain, Am. J. Surg. 31:351-353 (Feb.) 1936.

2. Abraham, V. R.: Injection of Alcohol in the Spinal Canal for Relief of Pain, Am. J. Surg. 39:317-318 (Aug.) 1935.

3. Adson, A. W.: Value of, and Indications for, Intraspinal Injections of Alcohol in Relief of Pain, Minnesota Med. 20:135-140 (March) 1937.

4. Aird, R. B., and Naffziger, H. C.: Experimental Injection of Ethyl Alcohol into the Lumbar Subarachnoid Space, with Neuropathological Studies, West. J. Surg. 43:377-387 (July) 1935.

5. Bonica, J. J.: The Management of Pain of Malignant Disease with Nerve Blocks, Anesthesiology 15:134-145 (March); 15:280-301 (May) 1954.

6. Campbell, E. H., Jr., and Whitfield, R. D.: Alleviation of Cancer Pain, J. Kansas M. Soc. (Supp.) 52:71A-74A (Sept.) 1951.

7. Dargent, M.: Role of Sympathetic Nerve in Cancerous Pain; Inquiry on 300 Cases, Brit. M. J. 1:440-442 (March 6) 1948.

8. Dogliotti, A. M.: Traitement des syndromes douloureux da la péripherie par l'alcoolisation sub-arachnoïdienne des racines postérieures à leur émergence de la moelle épinière, Presse méd. 39:1249-1252 (Aug.) 1931.

9. Dunphy, J. E., and Alt, R. E.: Relief of Pain by the Subarachnoid Injection of Alcohol, New England J. Med. 214:472-477 (March) 1936.

10. Fischer-Williams, M.: Treatment of Chronic Pain, Brit. M. J. 1:533-538 (March) 1956.

11. Gilcreest, E. L., and Mullen, T. F.: Epidural and Transsacral Injection of Alcohol for the Relief of Pain, S. Clin. North America 11: 989-994 (Oct.) 1931.

12. Grant, F. C.: Surgical Methods for Relief of Pain, Bull. New York Acad. Med. 19:373-385 (June) 1943.

13. Greenhill, J. P.: Relief of Pelvic Pain by Sympathectomy and Intraspinal Alcohol Injections, J. Internat. Coll. Surgeons 19:218-222 (March-April) 1947.

14. Greenhill, J. P., and Schmitz, H. E.: Intraspinal (Subarachnoid) Injection of Alcohol for

Pain Associated with Malignant Conditions of Female Genitalia, J. A. M. A. 105:406-409 (Aug. 10) 1935.

15. Groff, R. A.: Alcoholic Injections for Relief of Intractable Pain, S. Clin. North America 19:1569-1581 (Dec.) 1939.

16. Harney, C. H., and Kehres, H. N.: Relief of Intractable Pain by the Subarachnoid Injection of Alcohol, Pennsylvania M. J. 41:1117-1123 (Sept.) 1938.

17. Judovich, B., and Bates, W.: Pain Syndromes, Diagnosis and Treatment, Ed. 4, Philadelphia, F. A. Davis Company, 1953, pp. 314-327.

18. Labat, G.: Action of Alcohol on the Living Nerve: Experimental and Clinical Considerations, Current Res. in Anesth. & Analg. 12:190-196 (Sept.-Oct.) 1953.

19. Maher, R. M.: Relief of Pain in Incurable Cancer, Lancet 1:18-20 (Jan.) 1955.

20. Mandl, F.: Aqueous Solution of Phenol as a Substitute for Alcohol in Sympathetic Block, J. Internat. Coll. Surgeons 13:566-568 (May) 1950.

21. Olivecrona, H.: Surgery of Pain, Acta psychiat. & neurol. (Supp.) 46:268-280, 1947.

22. Olmsted, J. M. D., and Hodgson, P.: An Explanation of the Results of the "Alcohol Block," Am. J. Physiol. 97:597-601 (July) 1931.

23. Ottley, C.: Intrathecal Alcohol Injection for Relief of Pain: Review, Brit. M. J. 1:510-512 (March 5) 1938.

24. Owings, J. C., and Brantigan, O. J.: Use of Intraspinal Injection of Absolute (Dehydrated) Alcohol for Treatment of Intractable Pain, Bull. School Med. Univ. Maryland 21:145-150 (April) 1937.

25. Perese, D. M.: Spinothalamic Tractotomy in the Management of Pain of Malignant Disease, in preparation.

26. Peyton, W. T.: Semansky, E. J., and Baker, A. B.: Subarachnoid Injection of Alcohol for Relief of Intractable Pain, with Discussion of Cord Changes Found at Autopsy, Am. J. Cancer 30:709-717 (Aug.) 1937.

27. Pitts, W., and Browder, J.: Spinal Subarachnoid Injection of Absolute Alcohol for the Relief of Intractable Pain, Ann. Surg. 109:33-42 (Jan.) 1939.

28. Poppen, J. L.: Relief of Pain by the Use of Subarachnoid Alcohol Injection: Indications, Contraindications, Technic, and Results in 82 Patients, S. Clin. North America 16:1663-1668 (Dec.) 1936.

29. Russell, W. R.: Intraspinal Injection of Alcohol for Intractable Pain, Lancet 1:595-599 (March 14) 1936.

30. Russell, W. R.: Intraspinal Injection of Alcohol for the Relief of Intractable Pain, Tr. Med. Chir. Soc. Edinburgh, pp. 78-87, 1936-1937; in Edinburgh M. J., May, 1937.

31. Saltzstein, H. C.: Intraspinal (Subarachnoid) Injection of Absolute Alcohol, J. A. M. A. 103:242-243 (July) 1934.

32. Stern, E. L.: Relief of Intractable Pain by Intraspinal (Subarachnoid) Injection of Alcohol, Am. J. Surg. 25:217-227 (Aug.) 1934.

33. Stern, E. L.: Chronic Painful Conditions Amenable to Relief by Intraspinal (Subarachnoid) Injection of Alcohol, Am. J. Surg. 36:509-513 (May) 1937.

34. Trimble, I. R., and Morrison, S.: Treatment of Intractable Pain of Visceral Origin, J. A. M. A. 148:1184-1188 (April) 1952.

35. Truelsen, F.: Subarachnoid Alcohol Injection for the Relief of Intractable Pain, Acta chir. scandinav. 88:17-32, 1943.

36. Tureen, L. L., and Gitt, J. J.: Cauda Equina Syndrome Following Subarachnoid Alcohol Injection; Report of 2 Cases, J. A. M. A. 106:1535-1537 (May) 1936.

37. White, J. C.: A New Modification of Subarachnoid Alcohol Injection for the Bilateral Blocking of the Lower Sacral Nerves in Intractable Pain of the Pelvic Viscera, Surgery 4:722-727 (Nov.) 1938.

38. White, J. C., and Sweet, W. H.: Pain, Its Mechanisms and Neurosurgical Control, Ed. 1, Springfield, Ill., Charles C Thomas, Publisher, 1955, p. 245.

Ischemia of the Left Colon Associated with Abdominal Aortic Aneurysms and Their Treatment

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Since the advent of resectional therapy for abdominal aneurysms,[1,2] it has become evident that the inferior mesenteric artery can generally be divided close to the aorta with impunity. This fact was anticipated in many of the earlier reports of extirpation of aneurysms.[2-8] The hindgut derivatives usually remain viable under these circumstances because of the adequacy of collateral blood flow through the middle colic artery via the marginal artery of Drummond[9] and by a similar, but less effective and constant, flow through the middle hemorrhoidal arteries from below. This latter avenue of collateral blood supply presupposes that one hypogastric artery remains open. When the hypogastrics are occluded or must be sacrificed, such flow depends upon collateral channels through the inferior hemorrhoidal artery. The dimension of time may also play an ill-defined, and possibly not too important, role in the establishment of collateral circulation by these channels. Since many of the patients under discussion have generalized arteriosclerosis, they are subject, at least theoretically, to possible thrombosis of portions of the mesenteric blood supply either before or after surgical treatment.

There have been many excellent injection and ligation studies of the vascular anatomy of the colon, particularly with reference to the surgery of cancer.[9-16] These studies testify to the general adequacy of the marginal artery as a collateral channel. If one were to postulate an area of ischemic change in the descending colon subsequent to ligation of the inferior mesenteric artery, it would be in the area of the rectosigmoid, which has been shown by injection studies to be poorly endowed with collateral supply. The marginal artery is demonstrated with difficulty beyond the controversial "critical point of Sudeck."[17] Movius'[18] experience with resection of aneurysms included a very high incidence of postoperative diarrhea and two patients with rectal strictures 9 cm. from the anal margin, both of whom required later surgical treatment. Moore[19] reported a similar case, and both he and Movius suggested a possible causal relationship between this occurrence and resection of the abdominal aneurysm. Szilagyi,[20] in discussing the inadvisability of dividing the inferior mesenteric artery and concomitantly ligating both hypogastrics during resection of aneurysms, made a brief reference to two cases of "severe ischemia of the rectosigmoid colon" during temporary arterial occlusion. It is the purpose of the present report to describe two cases of ischemic changes in the left colon associated with arteriosclerotic abdominal aneurysms.

Report of Cases

CASE 1.—The patient was a 65-year-old white man who was first admitted to this hospital on Dec. 15, 1954, with a diagnosis of abdominal aneurysm. One month previously he had noted the onset of severe cramps and tenesmus while driving a tractor. He was admitted to another hospital, where exploratory laparotomy revealed an abdominal aneurysm and scattered localized areas of apparent gangrene of the transverse and descending colon. The abdomen was closed without definitive surgery. Postoperatively the patient had some watery and bloody bowel movements.

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He was then asymptomatic for two weeks prior to admission.

On Dec. 18, at operation, an abdominal aortic aneurysm was resected, and a Y-shaped graft of nylon filter fabric was interpolated between the aorta, above, and both common iliac arteries, below. The circulation to the entire colon appeared to be good at this time. Postoperatively he had some transient lobular atelectasis and abdominal cramps and distention. He made a good recovery and was discharged in apparently excellent condition two weeks after operation. Eight days later he was readmitted to his local county hospital with cramping abdominal pain, nausea, melena, and anemia. Transfusions were administered. Subsequent to this admission he continued to have alternating constipation and diarrhea.

Three months after his definitive surgery, and four months after the onset of his original symptoms, he was readmitted to our hospital with sigmoid obstruction 16 cm. from the anal orifice. Resection of the involved sigmoid was carried out. This portion of the colon was adherent to the lateral gutter, and a 4 mm. stricture associated with chronic, nonspecific ulceration was demonstrable.

The patient was readmitted to the hospital 11 months later because of fever of undetermined origin. A barium enema at this time revealed slight narrowing of the anastomotic site. He had no gastrointestinal symptoms. His fever subsided; he was discharged from the hospital and has remained well since then.

CASE 2.—The patient was an 82-year-old white woman who was admitted to the hospital on Oct. 18, 1956, with a 22-hour history referable to rupture of an abdominal aortic aneurysm. Though her normal blood pressure ranged around 210/100, on admission it was 140/90 and the pulse was 92 a minute. The hemoglobin was 9.4 gm. per 100 cc. There was a pulsating mass in the abdomen. The patient had been unconscious and in severe shock for a short time approximately three hours before admission. On exploration a ruptured abdominal aortic aneurysm was found. It was resected, and a straight nylon filter fabric graft was interpolated. A distal thromboendarterectomy was required. It was necessary to clamp the aorta above the renal arteries for 24 minutes early during the operation, which took slightly over 3 hours. The distal arteries pulsated well, and the left colon appeared to have good blood supply at the time of closure. A decompression tube gastrostomy was performed.

Her postoperative course was marked by confusion, oliguria, and hypotension. She pulled out her gastrostomy tube on the first postoperative day. During reinsertion of the tube, under local anesthesia, some dark, serosanguineous peritoneal fluid was encountered. It was thought that this represented residual bloody fluid from the original extravasation. The clinical course was a progressively downhill one, with irreversible shock, and ended in death 36 hours postoperatively. The femoral pulses were palpable until the time of death.

Postmortem examination revealed 50 cm. of the distal colon to be necrotic, and the mesenteric vessels were thoroughly occluded with a fresh thrombus. There were also small focal necrotic areas in the ileum and cecum. Generalized arteriosclerotic changes were present throughout the body.

Comment

Although it remains true that the inferior mesenteric artery can generally be divided without fear, there is a small risk involved. It is interesting that in the two cases of rectal stricture reported by Movius and the one reported by Moore the lesion occurred approximately 9 cm. from the anal margin, in the general area of the critical point of Sudeck. In our own case the stricture was situated only slightly farther from the anal orifice. Moore stated that both internal iliac arteries were ligated in his case and pointed out that there was no major blood supply to the colon distal to the middle colic artery. He presumed that the proctitis and stricture which developed were due to ischemia. Detailed information regarding the status of the hypogastrics was lacking in Movius' report, but he did state that one iliac artery became thrombosed postoperatively in one of his two cases. Szilagyi apparently avoided trouble in his patients, who exhibited ischemia following temporary occlusion of the hypogastric arteries.

The difficulty in one of our cases was due to thrombosis of the inferior mesenteric artery and some of the collaterals prior to operation. The situation may possibly have been aggravated by subsequent resection of the aneurysm. In the second case, that of an elderly woman with severe arteriosclerosis, the circulation was adequate at the time of completion of the operation and thrombosis of the collaterals ensued during the postoperative period.

It would seem evident that the hazard of necrosis of the colon is greater when it is necessary to ligate one or both hypogastric arteries and when generalized severe arteriosclerosis jeopardizes the maintenance of blood flow through the collateral vessels. The necessity for distal thromboendarterectomy, theoretically at least, might also increase this risk. The occurrence of diarrhea or of troublesome hypotension, or the presence of bloody abdominal fluid in the postoperative course, should make the surgeon aware of the possibility that ischemia of the left colon has occurred.

The area in the left colon in which a stricture may develop as the result of ischemic changes corresponds roughly to the critical point of Sudeck.

Conclusions

Difficulties with maintenance of adequate circulation to the left colon are occasionally encountered in association with arteriosclerotic abdominal aneurysms and their treatment. Two cases are presented and the pertinent literature reviewed.

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REFERENCES

1. Schafer, P. W., and Hardin, C. A.: The Use of Temporary Polythene Shunts to Permit Occlusion, Resection, and Frozen Homologous Graft Replacement of Vital Vessel Segments, Surgery 31:186-199, 1952.

2. Dubost, C.; Allary, M., and Oeconomos, N.: Resection of an Aneurysm of the Abdominal Aorta, A. M. A. Arch. Surg. 64:405-408, 1952.

3. Brock, R. C.: Aortic Homografting: A Report of 6 Successful Cases, Guy's Hosp. Rep. 102: 204-228, 1953.

4. DeBakey, M. E., and Cooley, D. A.: Surgical Treatment of Aneurysm of Abdominal Aorta by Resection and Restoration of Continuity with Homograft, Surg. Gynec. & Obst. 97:257-266, 1953.

5. Bahnson, H. T.: Treatment of Abdominal Aortic Aneurysm by Excision and Replacement by Homograft, Circulation 9:494-503, 1954.

6. Kirklin, J. W.; Waugh, J. M.; Grindlay, J. H.; Openshaw, C. R., and Allen, E. V.: Surgical Treatment of Arteriosclerotic Aneurysms of the Abdominal Aorta, A. M. A. Arch. Surg. 67:632-644, 1953.

7. Gerbode, F.; Parsons, H., and da Costa, I. A.: The Surgical Treatment of Abdominal Aortic Aneurysms: Report of Case Treated by Resection of Aneurysm with Restoration of Aorta by Homograft, Stanford M. Bull. 11:179-182, 1953.

8. Bahnson, H. T.: Excision of Arteriosclerotic Aneurysm of the Abdominal Aorta, Geriatrics 9: 263-271, 1954.

9. Drummond, H.: The Arterial Supply of the Rectum and Pelvic Colon, Brit. J. Surg. 1:677-685, 1914.

10. Braithwaite, J. L.: The Effects of Interruption of the Inferior Mesenteric Artery with Its Branches on the Blood Supply of the Terminal Part of the Large Gut in Experimental Animals, Surg. Gynec. & Obst. 100:521-531, 1955.

11. Steward, J. A., and Rankin, F. W.: Blood Supply of the Large Intestine: Its Surgical Considerations, A. M. A. Arch. Surg. 26:843-891, 1926.

12. Goligher, J. C.: The Blood-Supply to the Sigmoid Colon and Rectum, with Reference to Technique of Rectal Resection with Restoration of Continuity, Brit. J. Surg. 37:157-162, 1949.

13. Goligher, J. C.: Adequacy of the Marginal Blood-Supply to the Left Colon After High Ligation of the Inferior Mesenteric Artery During Excision of the Rectum, Brit. J. Surg. 41:351-353, 1954.

14. Grinnell, R. S., and Hiatt, R. B.: Ligation of the Inferior Mesenteric Artery at the Aorta in Resections for Carcinoma of the Sigmoid and Rectum, Surg. Gynec. & Obst. 94:526-534, 1952.

15. Ault, G. W.; Castro, A. F., and Smith, R. S.: Carcinoma of the Upper Rectum and Rectosigmoid: Clinical Report on High Inferior Mesenteric Ligation, Postgrad. Med. 8:176-183, 1950.

16. Ault, G. W.; Castro, A. F., and Smith, R. S.: Clinical Study of Ligation of the Inferior Mesenteric Artery in Left Colon Resections, Surg. Gynec. & Obst. 94:223-228, 1952.

17. Sudeck, P.: Über die Gefässversorgung des Mastdarmes in Hinsicht auf die operative Gangrän, München med. Wchnschr. 54:1314-1317, 1907.

18. Movius, H. J., II: Resection of Abdominal Arteriosclerotic Aneurysm, Am. J. Surg. 90: 298-305, 1955.

19. Moore, S. W.: Resection of the Abdominal Aorta with Defect Replaced by Homologous Graft, Surg. Gynec. & Obst. 99:745-755, 1954.

20. Szilagyi, D.; Smith, R. F., and Overhulse, P. R.: Resectional Surgery of the Abdominal Aorta, A. M. A. Arch. Surg. 71:491-511, 1955.

Endobronchial Hamartoma

Report of a Case

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Benign bronchial tumors are encountered with considerable rarity. In 283 bronchoscopic examinations performed at the Veterans' Administration Research Hospital during three and a half years only 1 example of this lesion has been found. None has been found on 622 routine autopsies. During this same period 186 bronchogenic carcinomas have been discovered clinically or at autopsy. It is difficult to determine the over-all incidence of benign bronchial tumors from the recorded literature, but it is probably in the vicinity of 1% if one excludes the so-called "benign" bronchial adenoma.

Clinically the most prominent feature of a benign endobronchial tumor is bronchial obstruction. This may be accompanied by atelectasis or obstructive pneumonitis. A persistent cough, and occasionally hemoptysis, may precede or accompany the symptoms of bronchial obstruction. In the older age group the clinical diagnosis prior to endoscopy is usually bronchogenic carcinoma.

The diagnosis of a benign bronchial tumor may be established often by bronchoscopic visualization and bronchial biopsy. However, not infrequently, owing to the location of the tumor, transthoracic exploration and resection are necessary to establish the diagnosis. If the tumor is recognized before irreversible pulmonary changes have developed distal to it, endoscopic removal is the preferred treatment. Occasionally, owing to the location of the lesion, a transthoracic bronchotomy is necessary to remove the tumor. When seen at a later stage, destructive changes in the parenchyma may necessitate a resection of the affected portion of the lung as well. Thus, as emphasized by Langston,[1] the importance of early removal of these tumors before the occurrence of irreversible changes is evident.

Numerous varieties of benign endobronchial tumors have been described. These include papilloma, fibroma, chondroma, lipoma, leiomyoma, myoblastoma, plasmocytoma, vascular malformations, and developmental tumors, i. e., hamartoma. Donoghue and associates[2] recently reviewed a series of 14 benign endobronchial tumors seen at the Mayo Clinic. The most frequent lesion found was the endobronchial hamartoma; five such cases were encountered. Their review of the literature disclosed 32 previously reported endobronchial hamartomas. A subsequent report by Bleyer and Marks[3] presents five additional cases. Atelectasis of the respective pulmonary segment was the prominent clinical feature in each instance. Bronchography, as well as bronchoscopy, was utilized as a diagnostic aid by these authors.

The endobronchial location of a hamartoma is considerably less frequent than its occurrence peripherally in the pulmonary parenchyma. However, it is one of the commoner benign tumors of the bronchus. Moreover, it is likely that many such lesions have not been reported or have not been classified as a hamartoma.

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Report of Case

A white man, 61 years of age, entered the Veterans' Administration Research Hospital on Feb. 11, 1957, with the chief complaints of persistent cough and hemoptysis. Five weeks before admission he noted the onset of cough, left subscapular chest pain, and associated chills and fever. He received penicillin and expectorants, with regression of the chills and fever, but the pain and cough persisted. The day prior to admission he expectorated a teaspoonful of bright red blood. A 5 lb. weight loss had been noted during the present illness. The past history revealed that for approximately the past 10 years he had had two or three attacks annually of similar respiratory complaints, but without hemoptysis. It was also noted that he had been a heavy smoker for many years.

Physical examination revealed no abnormal cardiorespiratory findings. Routine laboratory studies were within normal limits. A posterior-anterior roentgenogram of the thorax revealed an enlargement of the left hilus (Fig. 1). The left lateral roentgenogram of the chest disclosed an area of increased density in the region of the superior segment of the left lower lobe (Fig. 2). The roentgenologic findings were interpreted as atelectasis of the superior segment of the left lower lobe.

Bronchoscopy revealed a pink, glistening, polypoid mass that occluded the orifice to the left superior segmental bronchus. The mass was not friable, and no evidence of mucosal erosion was apparent. Multiple biopsy specimens were taken,

Fig. 1.—Posterior-anterior roentgenogram of the thorax showing prominence of the left hilus.

Fig. 2.—Lateral roentgenogram of the thorax showing atelectasis of the superior segment of the left lower lobe.

but it was impossible to remove the lesion completely. Histologic examinations of the biopsy tissues revealed normal bronchial mucosa with an underlying myxomatous stroma. The location of the lesion and the persistent atelectasis distal to it were felt to negate further attempts at endoscopic removal.

On Feb. 27, a left posterolateral thoracotomy was performed. Examination of the lung at operation revealed the superior portion of the left lower lobe to be contracted and firmly adherent to the overlying parietal pleura. The remainder of the lung appeared to be normal, as did the pulmonary hilus. The lung was freed, and a superior segmentectomy was performed. After division of the segmental bronchus a pedunculated tumor was readily identified arising from a narrow base on the inferior surface of the bronchial orifice. This was removed without difficulty. The adjacent main-stem bronchus appeared normal to direct visualization. The bronchial stump was closed with interrupted silk sutures and covered with adjacent tissue. The lung was reexpanded, the incision closed, and the hemithorax drained in the usual manner. The patient withstood the procedure without difficulty, and the postoperative course was uncomplicated.

Grossly the tumor was firm and resistant to sectioning. It measured 0.5×0.5 cm. in diameter. Histologically, there were lobulated areas of cartilaginous tissue within a mesenchymal stroma. The surface of the tumor was covered with normal bronchial epithelium (Fig. 3). The diagnosis of hamartoma of the bronchus was made.

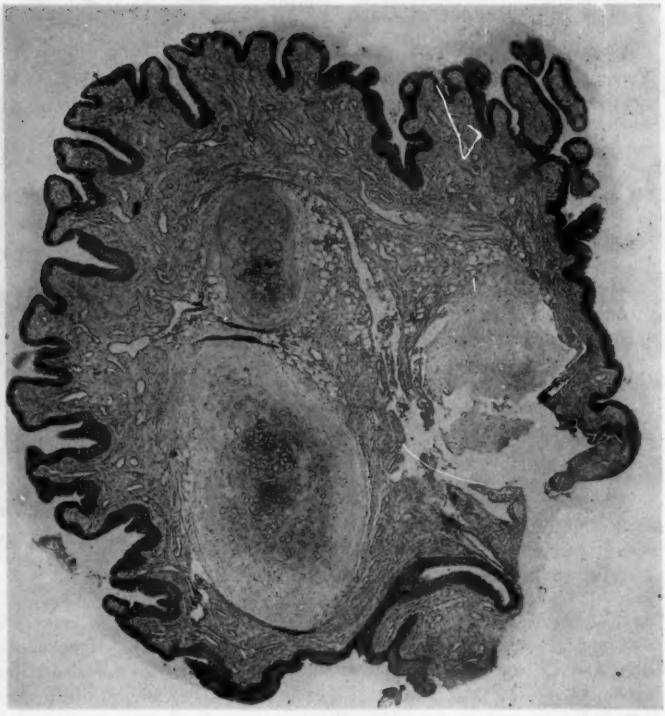

Fig. 3.—Photomicrograph of endobronchial hamartoma showing islands of cartilaginous tissue within a mesenchymal stroma. Reduced to ¾ of mag. × 18.

The patient's condition was reevaluated four months after operation and was asymptomatic. A roentgenogram of the thorax on June 25 revealed a completely reexpanded left lung, with minimal evidence of pleural changes at the left base.

Summary

Benign endobronchial tumors, although uncommon, are clinically important because they may produce bronchial obstruction and/or hemoptysis. In the older age group they are clinically indistinguishable from bronchogenic carcinoma. Fortunately, in the majority of instances the nature of the lesion can be determined by bronchoscopic visualization and biopsy. The technique of removal of a benign bronchial tumor is dependent not only upon its site of origin but also on whether or not permanent pulmonary changes have occurred distal to the tumor. In the absence of associated pulmonary pathology, endoscopic or transpleural bronchotomy removal is determined by the site of origin of the lesion. The presence of irreversible pulmonary changes requires some form of pulmonary resection. Conservation of as much normal lung tissue as possible should be an underlying principle in this instance.

A case of an endobronchial hamartoma is presented. This case illustrates the clinical and therapeutic features that have been discussed.

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REFERENCES

1. Langston, H. T.: Benign Endobronchial Tumors, Internat. Abstr. Surg. 91:521-535, 1950; in Surg. Gynec. & Obst., December, 1950.

2. Donoghue, F. E.; Andersen, H. A., and McDonald, J. R.: Unusual Bronchial Tumors, Ann. Otol. Rhin. & Laryng. 65:820-828 (Sept.) 1956.

3. Bleyer, J. M., and Marks, J. H.: Tuberculomas and Hamartomas of the Lung, Am. J. Roentgenol. 77:1013-1022 (June) 1957.

Biliary Dyskinesia in T-Tube Cholangiography

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The etiological factors accounting for symptoms persisting or following cholecystectomy for gallbladder disease can be classified as calculi in the biliary ducts,[1,2] stricture of the common duct,[3,4] surgical factors,[5] and re-formed gallbladder, with or without calculi.[6,7] Pericholedochal neuromata,[8] long cystic duct stump,[9] acute and recurring pancreatitis,[10] spasm,[10] fibrosis,[11] or anomalies of the sphincter of Oddi [12] have also been implicated. Other factors, namely, adhesions,[13] anomalies of the biliary and pancreatic ducts,[12] neoplasms of the ampulla of Vater,[14] bacterial sensitivity,[15] and psychosomatic elements [8] have also been mentioned. Upper abdominal symptoms following the use of sodium iodipamide (Cholagrafin)[16] in intravenous cholangiography have been reported.

The purpose of this paper is to report an additional factor that may be classified as chemical, namely, the use of sodium *o*-iodohippurate, as Medopaque-H. This radiopaque material has been responsible for the production of symptoms following cholecystectomy and associated T-tube cholangiography. The role of the hydrostatic pressure and/or irritating effects of contrast medium is discussed, since this may be a factor in the production of morbidity in those hospitals where T-tube cholangiography frequently is utilized.

Medopaque-H is a clear, stable viscous solution containing 35% sodium iodohippurate and, 10% sodium iodine with added stabilizers and preservatives. Polyethylene glycol is added for viscosity. The net iodine content of this material is 20%. This solution is miscible with body secretions, disperses uniformly, and produces dense, sharp shadows. It is completely absorbed from serous and mucous surfaces within 30 to 60 minutes following administration. At Jefferson Hospital contraindications for the use of Medopaque-H are iodine sensitivity, hyperthyroidism, and thyroid adenomas.

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Analysis of Cases and Source of Material

This study is based on clinical data obtained from records of patients who had cholecystectomy and choledochostomy performed for acute and chronic cholecystitis with or without cholelithiasis, during the period Jan. 1, 1956, to June 30, 1956. Of the total number of 64 cholangiographic procedures, 36 were the T-tube and 28 were the intravenous type. Ten patients (30.6%) developed complaints referable to the biliary system incident to T-tube cholangiography. Clinical data and cholangiograms were obtained from the departments of surgery and radiology at the Jefferson Medical College Hospital. Following cholecystectomy and choledochotomy, a T-tube was placed in the common bile duct after exploration and evacuation of any stones. Eight to fourteen days after operation, the patients were sent to the department of radiology for T-tube cholangiography. Of 36 patients in this series, 10 developed severe reactions, i. e., colicky abdominal pain and symptoms mimicking an acute pancreatic or biliary lesion, immediately following injection of the contrast media, or shortly thereafter.

In cases with severe reactions, it was necessary to discontinue the procedure until a later date with the same or some other radiopaque material. When the study was repeated with Medopaque-H, severe reactions again occurred. Such a practice is time-consuming to the surgeon and the radiologist and achieves an added morbidity and expense to the patient requiring extended hospitalization.

Clinical Data

Of the total number of 10 cases developing biliary dyskinesia associated with T-tube cholangiography, 7 are reported, and all patients were of the white race. There were five women and two men, ranging in age from 51 to 71 years. Three of the total number of cases studied presented similar findings and therefore were not included in this report.

Report of Cases

CASE 1.—This 55-year-old white woman was admitted to the hospital on Jan. 4, 1956, complaining of severe epigastric and right upper quadrant abdominal pain, nausea, and vomiting of several hours' duration. A previous episode of symptoms referable to the biliary tract occurred seven months earlier. On admission the temperature was 103.6 F, the pulse 100 a minute, respirations 22 a minute. There were moderate distention, tenderness, and rebound tenderness over the right upper quadrant of the abdomen. The leukocyte count was 15,400 per cubic millimeter, and liver function studies were within normal limits.

The patient was treated conservatively with nasogastric suction, intravenous fluids, and antibiotics. Several days later, after symptoms had subsided, an upper gastrointestinal series and cholecystographic examination were done, on Feb. 1 and 4, and reported as normal. However, on the basis of the clinical symptoms, the abdomen was explored, and cholecystectomy, choledochostomy, and liver biopsy were done for chronic noncalculous cholecystitis and chronic cholangitis. Two days after operation there developed sustained substernal pain, hypotension, and evidence of a left bundle-branch block, which was confirmed by electrocardiographic tracings. The QRS complexes were deflected up in Lead I and slurred, and deflected down in Lead III, with an interval greater than 12 seconds.

Thereupon the patient was placed on a medical regimen and made an uneventful recovery. On Feb. 13, or 13 days subsequent to operation, T-tube cholangiography, using Medopaque-H was done. Ten centimeters of Medopaque-H was inserted into the T-tube. The cholangiogram appeared normal, and there was partial filling of the duct of Wirsung.

Shortly after returning to the ward, this woman suddenly developed right upper quadrant pain, radiating through to the back and localizing between the intrascapular area. There was associated nausea and vomiting.

Upon examination, the abdomen was found to be tender in the right upper quadrant. With analgesics and antispasmodics, pain subsided the following day, and the T-tube was clamped and removed on Feb. 16, 1956.

CASE 2.—This 57-year-old white man was admitted to Jefferson Hospital on Feb. 6, 1956, with recurrent pain in the right upper abdominal quadrant, radiating to the back. He gave a nine-year history of symptoms compatible with gallbladder disease, and intolerance to fried, fatty, or greasy foods. Food and alkali accentuated the abdominal pain. Three and one-half months previously the patient had been hospitalized and treated conservatively for an active duodenal ulcer, the diagnosis being confirmed radiologically.

On admission, there were tenderness in the right upper quadrant of the abdomen and a moderate degree of muscle guarding, and the liver was palpable 2 fingerbreadths below the right costal margin. Cholecystography demonstrated nonvisualization of the gallbladder. In the biliary drainage calcium bilirubinate crystals were found. On Feb. 18, the patient was operated upon. The gallbladder was chronically inflamed, and there were calculi in the common bile duct. Choledochotomy, cholecystectomy and T-tube insertion were done.

On March 1, 1956, or 12 days postoperatively, 10 cc. of Medopaque-H was injected into the T-tube, and there was no evidence of obstruction to flow or reflux. Following injection, there was marked upper abdominal pain, which radiated through to the back. The patient became nauseated and vomited several times and appeared cold, clammy, and pale, with a fast, thready pulse. Clinically he appeared to have acute pancreatitis. This was confirmed by a serum amylase of 2000 Somogyi units. The patient was treated with nasogastric suction, antispasmodics, analgesics, and antibiotics. Profuse drainage of bile appeared around the T-tube; but two days later the T-tube was removed, and he made an uneventful recovery and was discharged on March 23, 1956.

CASE 3.—On Feb. 18, 1956, this 55-year-old white woman, with a history of multiple thyroidectomies for thyrotoxicosis, a record of cardiac disease, and generalized arteriosclerosis, was admitted to Jefferson Hospital complaining of anorexia, nausea, weight loss of 20 lb. (9 kg.) in one month, and right upper quadrant pain. Three weeks prior to admission there were intermittent bouts of nausea and sharp right upper quadrant pain, radiating to the right scapular area subsequent to ingestion of food. She gave no history of jaundice or acholic stools.

Pertinent laboratory studies revealed a serum bilirubin of 1.3 mg. per 100 cc., a sulfobromophthalein retention of 18%, and an alkaline phos-

phatase of 3.75 mg. per 100 cc. Cholecystography demonstrated calculi in the gallbladder, and EKG showed some nonspecific myocardial changes.

On March 15 cholecystectomy and choledochotomy with T-tube drainage of the common bile duct were done for acute calculus cholecystitis.

On March 22, seven days postoperatively, 10 cc. of Medopaque-H was instilled through the T-tube into the extrabiliary duct system. Because of small stones present in the distal end of the common duct, cholangiography was repeated on March 26 and March 29. On March 26, following the injection of 20 cc. of the radiopaque medium, the patient complained of a heavy pressure sensation, fullness, and discomfort in the right upper quadrant of the abdomen. Fever and leukocytosis were present, but there was no laboratory evidence of pancreatitis. The T-tube was left open for drainage, and these symptoms subsided within a few days.

On April 16 a repeat cholangiography with 10 cc. of Medopaque-H was done, and the upper abdominal pain and sensation of pressure was so severe that the contrast material had to be aspirated through the stem of the T-tube and the examination terminated. The T-tube remained clamped for 10 days longer, at which time the patient was asymptomatic and there was no further evidence of bile spillage.

CASE 4.—This 51-year-old white woman was admitted on April 24, 1956, for evaluation and treatment of right upper quadrant abdominal pain and nausea of several weeks' duration. There were tenderness to palpation over the right upper quadrant and increased muscle resistance. There was a 15% sulfobromophthalein retention, and cholecystography, done on April 26, demonstrated multiple faceted stones. On May 1 cholecystectomy and common-duct exploration were performed for calculus cholecystitis. Nine days later, when 8 cc. of Medopaque-H was introduced into the T-tube, the patient's original symptoms were produced, i. e., biliary colic, cold clammy skin, and a fast and thready pulse. Under fluoroscopy this contrast medium was seen to regurgitate into the ducts of Wirsung. After 24 hours the symptoms subsided, and the T-tube was removed two days later. The patient was discharged on May 19 in an asymptomatic state.

CASE 5.—This 56-year-old white woman was admitted on April 26, 1956, with right upper quadrant abdominal pain, radiating along the right costal margin into the back. There were associated nausea and vomiting. She also gave a history of intolerance to fried and fatty foods. A cholecystogram taken three years previously demonstrated calculi in the gallbladder.

The abdomen was tender, with moderate rebound tenderness over the upper abdomen, especially the right upper quadrant. Cholecystography showed evidence of cholelithiasis, and the common bile duct was packed with stones of similar size. Cholecystectomy and transduodenal choledochotomy were done for calculus cholecystitis. Calculi at the origin of the right hepatic duct could not be evacuated, owing to the patient's poor condition during operation, after the gallbladder was removed. On May 8, the biliary radicals appeared normal after T-tube cholangiography and some reflux of the opaque material around the T-tube in the gallbladder bed, and poor filling of the common duct was noted. On May 16, nine days later, 15 cc. of Medopaque-H was injected into the T-tube. Visualization of the common bile and hepatic ducts was good. Two or three hours later she suddenly developed upper abdominal discomfort, became nauseated, and vomited on two occasions.

On June 18, a T-tube cholangiogram demonstrated that the calculus in the right hepatic duct had migrated down into the common duct, opposite the upper limb of the T-tube.

CASE 6.—This 71-year-old white woman was admitted on May 22, 1956, with signs and symptoms referable to the biliary tract. There was tenderness to palpation over the right upper quadrant of the abdomen. The liver was slightly enlarged. A cholecystogram revealed a large noncalcified stone in the fundus of the gallbladder. On May 24, the patient was operated upon, and calculi were found in the gallbladder. Cholecystectomy was done, and upon exploration of the common bile duct no calculi were found. A T-tube was inserted in the common duct. On June 4, 1956, T-tube cholangiography demonstrated good visualization of the common and hepatic ducts, but slight extravasation of opaque material around the gallbladder bed was noted. The T-tube was clamped the next day, and a few hours later she began complaining of discomfort in the right upper quadrant, with anorexia and nausea. The following morning, two days after cholangiography, symptoms were progressive, and abdominal pain had become generalized. The temperature rose to 103 F; the pulse was 120; respirations were 22, and there were generalized abdominal tenderness and rebound tenderness. For the next three to four days the clinical course remained the same. She was treated with nasogastric suction, intravenous fluids, amino acids, and antibiotics. A serum amylase determination five days after initial episode was less than 80 Somogyi units. On June 15, an upper gastrointestinal series showed evidence of obstruction at the second portion of the duodenum.

On June 18, exploration was done, and examination of the pancreas established the obstruction as due to acute pancreatitis, primarily implicating the

head of the pancreas. A gastroenterostomy was established, and her postoperative course exhibited progressive improvement. Twenty-eight days following the second operative procedure, a wound dehiscence developed. The wound was closed with heavy No. 28 wire through-and-through stay sutures. She made a slow, but complete, recovery.

CASE 7.—This 58-year-old man was admitted on June 16, 1956, complaining of indigestion, intermittent, colicky right upper quadrant abdominal pain, nausea, and vomiting of two days' duration. He had generalized tenderness, rebound tenderness, and muscle guarding. The leukocyte count was 13,100, with a differential count of 75% segmented cells, 9% nonsegmented cells, 13% lymphocytes, and 3% monocytes. He was treated conservatively until June 26, when a cholecystectomy and common-duct exploration were performed. At operation no calculi were found, but a T-tube was inserted in the common duct. Ten days after cholecystectomy, a T-tube cholangiography was done with Medopaque-H. It revealed a complete obstruction of the distal portion of the common duct, suggesting the presence of an impacted stone at this point. Contrast medium entered the duct of Wirsung, and the patient complained bitterly of upper abdominal pain. No contrast medium appeared to pass into the duodenum and the distal end of the common duct was narrowed, but under fluoroscopy there was noted some retrograde flow up into the main pancreatic duct. In 24 hours the abdominal pain subsided and one week later, on July 2, a repeat cholangiogram with iodized oil U. S. P. (Lipiodol) was normal. The T-tube was removed and the patient was discharged asymptomatic on July 5, 1956.

Summary and Conclusions

The etiological factors responsible for the persistence of symptoms following cholecystectomy are mentioned.

An additional agent contributing to biliary dyskinesia is referred to as the chemical factor Medopaque-H, a clear, aqueous, stable, radiopaque medium, containing sodium *o*-iodohippurate, in 10% sodium iodide with polyethylene glycol, which has been utilized in T-tube cholangiography following cholecystectomy and choledochostomy.

Of 36 patients who had T-tube cholangiograms with this material, 10 developed biliary dyskinesia. Seven of these cases have been reported in detail. Five of the seven had evidence of pancreatitis. The association of chemical cholangitis and possible calculus probably accounts for the symptoms in Case 2 and Case 5.

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REFERENCES

1. Walters, W.: Postcholecystectomy Dyskinesia, with Pancreatitis, Sphincteritis, and Choledocholithiasis as Causes, J. A. M. A. 160:425-431 (Feb.), 1956.

2. Millbourn, E.: On Re-Operation for Choledocholithiasis, Acta chir. Scandinav. 99:285, 1949.

3. Cole, W. H.; Ireneus, C., and Reynolds, J. T.: Strictures of the Common Duct, Ann. Surg. 133:684, 1951.

4. Massie, F. M.: Longmire Operation for Common Duct Obstruction, Ann. Surg. 131:838, 1950.

5. Hodge, J., and Hodge, G. B.: Post-Cholecystectomy Syndrome, J. South Carolina M. A. 51: 40, 1955.

6. Peterson, F. R.: Re-Formed Gallbladder: Review of 42 Cases, J. Iowa M. Soc. 36:134, 1946.

7. Bauer, W. B. A. J.: Postcholecystectomy Complicated Due to Incomplete Removal of the Gallbladder and Cystic Duct, A. M. A. Arch. Surg. 63:612, 1951.

8. Womack, N. A., and Crider, R. L.: The Persistence of Symptoms Following Cholecystectomy, Ann. Surg. 126:31, 1947.

9. Garlock, J. H., and Hurwitt, E. S.: The Cystic Duct Stump Syndrome, Surgery 29:833, 1951.

10. Doubilet, H., and Mulholland, J. H.: The Surgical Treatment of Recurrent Acute Pancreatitis by Endocholedochal Sphincterotomy, Surg. Gynec. and Obst. 86:295, 1948.

11. Cattell, R. B., and Colcock, B. P.: Fibrosis of the Sphincter of Oddi, Ann. Surg. 137:797, 1953.

12. Cole, W. H., and Grove, W. J.: Persistence of Symptoms Following Cholecystectomy with Special Reference to Anomalies of the Ampulla of Vater, Ann. Surg. 136:73, 1952.

13. Lovell, S. H.: Unsatisfactory Results After Cholecystectomy, M. J. Australia 1:644, 1956.

14. Cattell, R. B., and Pyrtek, L. J.: Premalignant Lesions of the Ampulla of Vater, Surg. Gynec. & Obst. 90:21, 1950.

15. Jennings, W. K.; Ortega, L. R., and Braslow, L.: Relationship of Postcholecystectomy Disturbances to Bacterial Sensitivity, Surg. Gynec. & Obst. 95:439, 1952.

16. Sandweiss, D. J., and Fulton, H.: Intravenous Cholangiography: Results in 100 Cholecystectomized Patients with Upper Abdominal Symptoms, J. A. M. A. 159:998, 1955.

Potassium, Magnesium, and Neostigmine for Controlled Cardioplegia

Evaluation with the Isolated Perfused Cat Heart

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During open-heart surgery there is much to be gained from having a still heart. The danger of air embolism is minimized; blood loss is lessened, and the surgeon has a clearly visible and motionless operative field. The presumed tolerance of the still heart to ischemia might be still another important advantage. In hypothermia, operations on the ventricles would not be feasible without a method of control of the heart action.

Certain ions have long been known to have cardioplegic properties. Ringer[1] discovered in 1883 that an excess of potassium is capable of stopping the heart in diastole and that an excess of calcium can do so in systole. Hooker,[2] Wiggers,[3] and, more recently, Swan[4] have injected potassium salts into the coronary circulation in order to stop ventricular fibrillation. Inhibition of cardiac contractions by the injection of potassium chloride, acetylcholine, methacholine chloride U. S. P. (acetyl-β-methylcholine chloride; Mecholyl), and related compounds into the coronary circulation was sought by Senning,[5] but his attempts were unsuccessful, probably because the agents were washed out or diluted by the continued coronary perfusion. Lam and associates[6] experimented with potassium chloride in the hypothermic intact dog but discarded this solution because potassium chloride produced fibrillation during the recovery period. Melrose[7] and his co-workers successfully produced cardiac arrest and recovery in the isolated dog heart as well as in the intact animal with the intracoronary injection of potassium citrate. In our laboratory, we have reported on the use of potassium, magnesium, and neostigmine (Prostigmin) in the intact dog.[10] Finally, cardioplegic agents have been applied to human surgery, utilizing potassium salts,[8] acetylcholine,[9] and a potassium, magnesium, and neostigmine mixture.[10]

The object of this report is to describe our studies of various cardioplegic agents and to record evidence for the superiority of the potassium, neostigmine, and magnesium combination in the isolated perfused cat heart.

Method

A healthy cat of either sex was anesthetized with 30-60 mg. of pentobarbital sodium U. S. P. injected intraperitoneally. The chest was opened and the inferior vena cava, superior vena cava, pulmonary artery, and aorta were clamped, in that order. The heart was immediately removed from the body and submerged in modified Ringer's solution[12] at a temperature of 0 C. The entire procedure, from the initial incision to immersion in the cold solution consumed about 1.5 minutes. As soon as the heart beat ceased, the pericardium was stripped from the heart and great vessels and a cannula was tied into the proximal end of the cut ascending aorta. The heart was then perfused through the cannula with the modified Ringer's solution at a temperature of 37.5 C according to the method of Langendorff.[13] After allowing 10-15

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minutes of a regular beat, the infusion stream was stopped, and 10 ml. of solution containing the specified amount of the drug to be tested was injected into the cannula in such a way as to perfuse the coronary arteries. After the heart stopped, it was allowed to remain without perfusion for 10 minutes. The perfusion was then resumed and allowed to continue until 10-15 minutes of a good, vigorous beat was obtained before additional tests were made. When the results may have been influenced by the order of testing, the sequence was varied on one or more new hearts. All drugs were tested on at least two different preparations. No drug or combination was used more than three times on any given heart except in the cases specifically noted in the text. All solutions were also tested with the heart and perfusates at a temperature of 28 C. The only difference noted between the hot and the cold environment was a slight prolongation of time (0.5-1.0 minute) required to return to a normal beat when the cooled system was used.

Electrocardiographic electrodes either were connected directly to the heart (aorta and cardiac apex) or were placed in the vessel surrounding the isolated heart. Contractility was measured by means of a muscle lever connected by a thread sutured into the muscle at the cardiac apex.

Results

Several groups of drugs were tested. Particular attention was paid to acetylcholine and the parasympathomimetic drugs because of the beneficial effects anticipated during hypothermic surgery and the ease of inducing recovery with atropine.[4]

The parasympathomimetics, methacholine and carbachol U. S. P. (carbamylcholine; Doryl) and others tested (Table 1) were found to slow the heart rate and decrease the electrocardiographic potential in an irregular and incomplete manner. Concentrations of acetylcholine chloride (10^{-3} M and 10^{-2} M), as used by Lam[14] and by Moulder,[15] caused the rate to be significantly slowed but did not induce complete electrical or muscular arrest. Atropine caused prompt

TABLE 1.—*Effect of Various Substances on the Isolated Cat Heart at 37 C*

Drugs Injected at 37.5 C in 10 Cc. Modified Ringer's Solution	Time for Maximum Effect, Min.	EKG 10 Min. After Injection	Time to Regain Strong Beat, Min.	EKG After Recovery
20 mg. acetylcholine	0.6	Slow rate; increased amplitude; depressed ST segments; eventual bundle branch block	2	Depressed ST segment; inverted QRS, alternating with upright QRS inverted P-waves; 0.05 mg. of atropine reverted
0.2 mg. carbachol *	0.5	Irregular potential of less than 0.1 mv.	0.6	No effect
50 mg. methacholine chloride	--	Slight decrease in amplitude of QRS for 3-4 beats	--	No effect
40 mg. pilocarpine	2.0	Irregular potential of 0.5 mv. spaced 1 min. apart	0.6	Inverted QRS; depressed ST segment with AV block for 3-4 min.
0.75 mg. neostigmine	0.3	Irregular potential of less than 0.1 mv.	3.3	No effect
20 mg. edrophonium chloride ‡	--	Slightly depressed ST segment	--	No effect
10 mg. bethanechol chloride §	--	No effect	--	No effect
25 mg. atropine	--	Irregular potential of 0.5 mv.	4	Widened QRS; depressed ST segment; flattened P-waves
Anoxia (no perfusate)	4			Slows beat; AV block; injury pattern; no arrest
12.5 mg. antazoline HCl ‖	1.7	Irregular potential of 0.5 mv.	10.1	Inverted widened QRS; depressed P-waves
25 mg. diphenhydramine HCl ¶	Immediate	Irregular potential of less than 0.01 mv.	0.6	No effect
8 mg. chlorpheniramine maleate #	0.8	Irregular potential of less than 0.5 mv.	2.0	No effect
20 mg. methapyrilene HCl **	Immediate	Irregular potential of less than 0.1 mv.	3.0	No effect
25 mg. cyclizine HCl ††	0.6	Irregular potential of less than 0.5 mv.	--	Never recovered
25 mg. tripelennamine citrate ‡‡	1.0	Irregular potential of less than 0.01 mv.	0.6	No effect
100 mg. amobarbital sodium §§	4.0	Irregular potential of less than 0.01 mv.	0.3	No effect
10 mg. pentobarbital sodium ‖‖	3.0	Irregular potential of less than 0.5 mv.	8.5	No effect
50 mg. secobarbital sodium ¶¶	2.5	Irregular potential of less than 0.1 mv. with occasional P-wave	4.0	No effect
10 mg. thiamylal sodium ##	1.75	Irregular potential of less than 0.5 mv.	10.75	No effect

* Doryl.
† Mecholyl chloride.
‡ Tensilon chloride.
§ Urecholine chloride.
‖ Antistine hydrochloride.
¶ Benadryl hydrochloride.
# Chlor-Trimeton maleate.
** Histadyl hydrochloride.
†† Marezine hydrochloride.
‡‡ Pyribenzamine citrate.
§§ Amytal sodium.
‖‖ Nembutal sodium.
¶¶ Seconal sodium.
Surital sodium.

resumption of a normal rate, rhythm, and electrocardiographic pattern.

Because antihistaminic drugs have been used as antifibrillatory agents,[16] we tested several (Table 1) of these. Diphenhydramine (Benadryl) hydrochloride, methapyrilene U. S. P. (Histadyl), and tripelennamine (Pyribenzamine) hydrochloride slowed the cardiac rate and decreased the electrocardiographic amplitude to less than 0.5μv. After the drugs were perfused out of the coronary circulation, the electrocardiographic pattern returned to normal. These same effects were noted with the barbiturates, amobarbital (Amytal) sodium, pentobarbital (Nembutal) sodium, secobarbital (Second) sodium, and thiamylal (Surital) sodium (Table 1).

Both potassium and magnesium salts caused complete cessation of cardiac activity when perfused through the coronary circulation in sufficient concentration. These ions were therefore combined in various proportions (Table 2) in order to determine the presence of any synergistic effect, particularly with respect to the production of prompt cardiac arrest, and a rapid return to a normal beat on reperfusion with the maintenance solution. A solution containing 2.47% gm. of hydrated magnesium sulfate ($MgSO_4 \cdot 7H_2O$) per 100 cc. and 0.81 gm. of potassium citrate ($K_3[C_6H_5O_7]H_2O$) per 100 cc. was found to be the most effective of those tried, especially in regard to speed and completeness of recovery. Using this solution, it was possible to stop and start the heart nine times over a three and one-half hour period without evidence of damage other than slight decrease in force of contraction and an alteration in the S-T segment, changes which might be secondary to the edema that invariably occurs after a time in these preparations. Neither potassium nor magnesium individually was as effective (Table 2).

Table 2 would indicate that isotonic $MgSO_4$ or $MgCl_2$ solutions are the preferred solutions. However, it was noted that when these were used repetitively on the same heart, ectopic beats began to appear and increased in number. This did not occur in the magnesium-potassium combinations, which were therefore deemed best for trial in dogs despite the slightly longer time for recovery after reperfusion. The addition of a small quantity of an antifibrillatory drug has no adverse effect on the cardioplegic properties of the solution.

The effect of the citrate ion, which is known to be a calcium-chelating agent, was investigated by the use of equivalent values of chloride and citrate in combination with potassium and magnesium. The cardioplegic effect was not apparently affected by the change.

TABLE 2.—*Effect of Perfusing the Isolated Cat Heart with Various Drugs at 37.5 C*

Solution	No. Trials	Time to Resume Beat, Min.		Number That Fibrillated After Standstill
		1st Beat	Regular Rate	
1.12% KCl 150 mEq. 300 mM.	6	1.9	2.6	1
1.6% K Cit. 150 mEq. 200 mM.	7	1.8	3.1	Two showed no fibrillation but died almost immediately after recovery
2.42% K Cit. 225 mEq. 300 mM.	11	2.5	3.8	--
2.03% $MgCl_2$ 200 mEq. 300 mM.	4	0.5	1.7	--
2.46% $MgSO_4$ 200 mEq. 200 mM.	4	1.5	2.4	--
3.69% $MgSO_4$ 300 mEq. 300 mM.	21	0.8	1.9	--
$MgSO_4$ 200 + K Cit. 50 mEq. 200 67 mM.	16	0.3	1.7	3
$MgSO_4$ 100 + K Cit. 150 mEq. 100 200 mM.	2	1.9	5.6	--
$MgSO_4$ 200 + K Cit. 75 mEq. 200 100 mM.	15	1.5	3.5	--

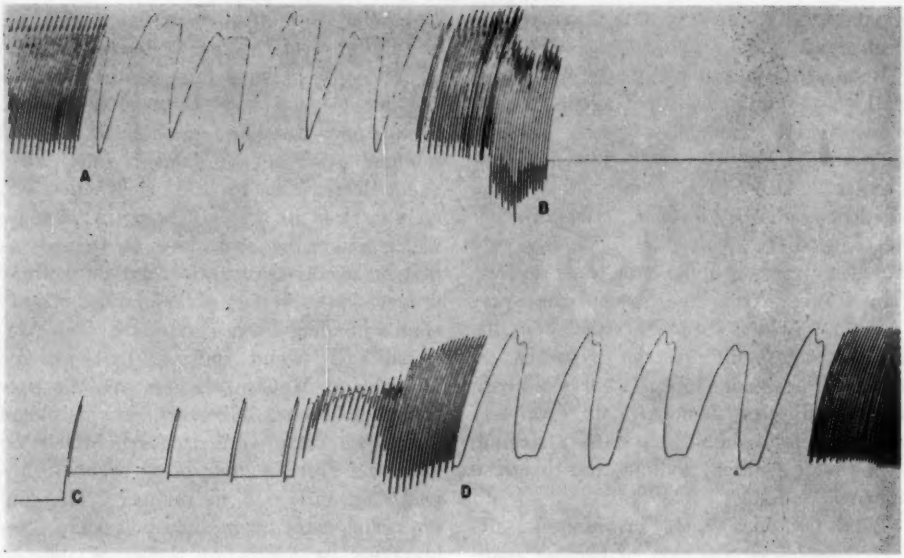

Fig. 1.—Effect on heart-muscle contractility of 10 ml. of 2.42% hydrated potassium citrate. *A*, pattern before injection; *B*, pattern during injection of material; *C*, first beat after 10 minutes of cardioplegia; *D*, pattern after normal beat is established by reperfusion.

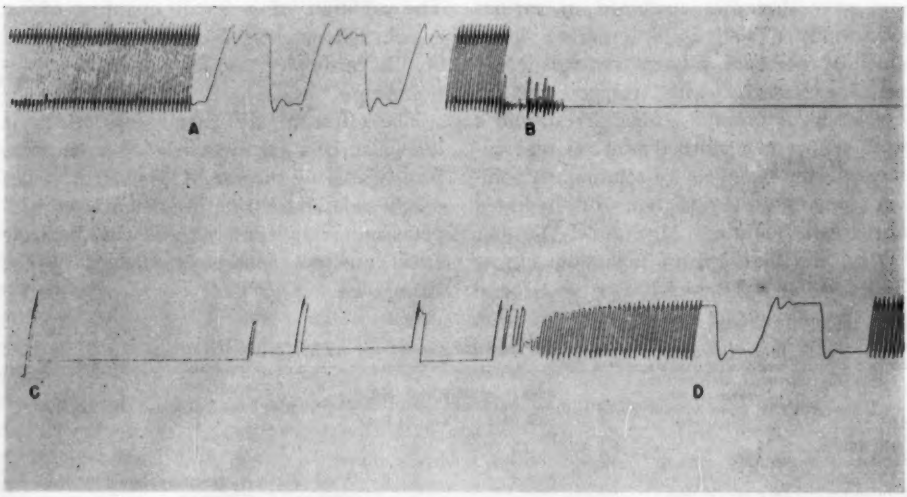

Fig. 2.—Effect on heart-muscle contractility of 10 ml. of 3.69% hydrated magnesium sulfate. *A*, pattern before injection; *B*, pattern during injection of material; *C*, first beat after 10 minutes of cardioplegia; *D*, pattern after normal beat is established by reperfusion.

Figures 1 to 3 reproduce myographic tracings, and Figure 4 shows electrocardiographic tracings made before, during, and after injection of the cardioplegic agents into the coronary circulation. This demonstrates the cessation of muscular and electrical activity and the return to the original myographic and electrocardiographic pattern on reperfusion.

Comment

The ideal solution for producing cardioplegia for surgery should have the following characteristics: rapid induction of cardiac arrest, absence of electrical and muscular

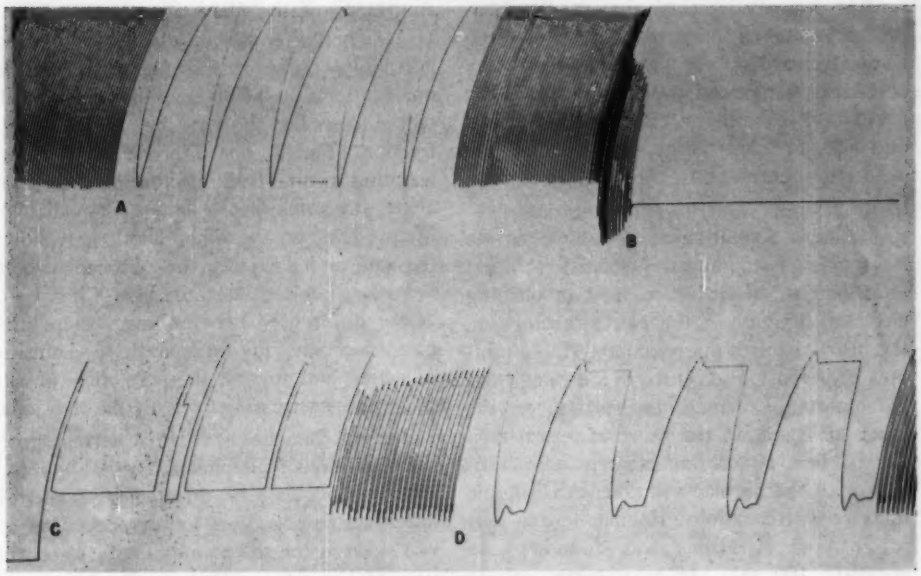

Fig. 3.—Effect on heart-muscle contractility of 10 ml. of 2.47 gm. of hydrated magnesium sulfate and 0.8 gm. of hydrated potassium citrate per 100 cc. solution. *A*, pattern before injection; *B*, pattern during injection of material; *C*, first beat after 10 minutes of cardioplegia; *D*, pattern after normal beat is established by reperfusion.

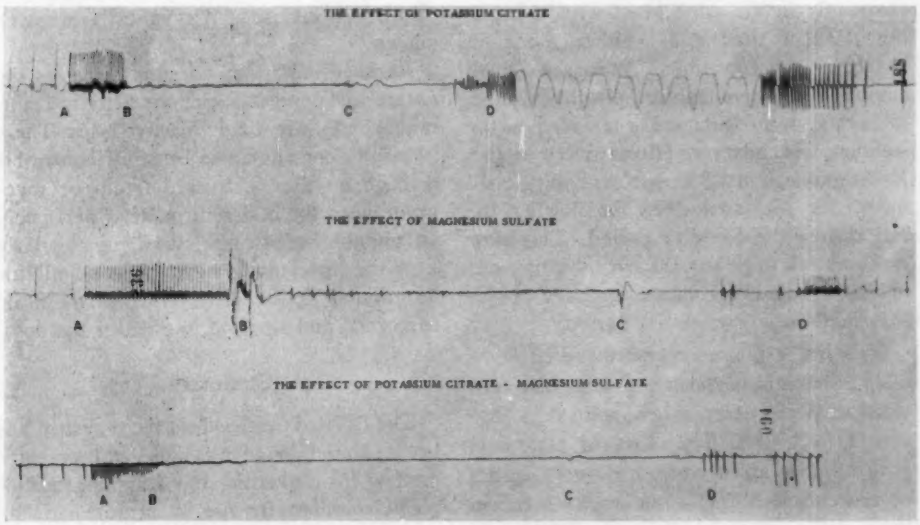

Fig. 4.—Electrocardiographic changes induced in heart muscle by various cardioplegic agents: 10 ml. of 2.42% hydrated potassium citrate; 10 ml. of 3.69% hydrated magnesium sulfate, and 10 ml. of 2.47 gm. of hydrated magnesium sulfate and 0.81 gm. of hydrated potassium citrate per 100 cc. solution. *A*, pattern before injection; *B*, pattern during injection of material; *C*, first beat after 10 minutes of cardioplegia; *D*, pattern after normal beat is established by reperfusion.

cardiac activity during the cardioplegia, minimal metabolic activity, rapid resumption of normal cardiac beat on reperfusion of the coronaries with blood, absence of ventricular fibrillation or other serious arrhythmias, and lack of toxicity if the entire cardioplegic dose gains entrance to the general circulation.

Although a solution of potassium citrate is capable of stopping the isolated cat heart immediately on injection and abolishing electrical activity in the electrocardiogram, the heart requires approximately three minutes of perfusion to return to a normal beat. A solution of magnesium sulfate, on the other hand, allows the heart to return to a normal beat almost immediately on perfusion with the regular solution. An isotonic mixture with a ratio of 100 magnesium ions to 75 potassium ions was found to be optimal (100 mM. of magnesium sulfate and 25 mM. of potassium citrate per liter). This combination caused immediate cardioplegia and rapid recovery on reperfusion. Furthermore, it was found that the combination which contained smaller concentrations of both ions could be used more frequently in the same heart without causing damage than could either alone in stronger concentration. When a small amount of tripelennamine, diphenhydramine, carbachol, or neostigmine was added to the solution, no adverse effects were noted. Neostigmine is used in our cardioplegic solution for its vagal effect in slowing the rate during the recovery period. This slow rate was felt to be particularly advantageous in that it allowed efficient coronary perfusion in the early wash-out period.

It is interesting to compare the effect of magnesium and potassium on muscular contraction of the heart, as exemplified in Figures 1 to 3. The first effect of potassium is to produce an increase in diastolic length of the muscle fibers, as shown by a fall in the base line at *B* in Figure 1. The extent of the fiber contraction remains almost the same until complete failure of the beat. On reperfusion, there is a marked diastolic shortening of the fibers after the first beat (*C*). Thereafter, action quickly returns to normal (*D*). In contrast, magnesium does not appreciably affect the diastolic length of the fibers but shortens the extent of contraction (Fig. 2, *B*). Electrically, it is interesting to note that injection of potassium alone stops the heart almost immediately. Magnesium, on the other hand, first slows the rate and abolishes the ventricular beat before complete cardioplegia (Fig. 4). These differences between magnesium and potassium may indicate separate mechanisms of action and suggest the possibility of additive or synergistic effects of the two ions.

The mechanism of cardiac arrest with these solutions is unknown. Excitability and contractility may be affected by (1) the difference in potassium ion concentration on two sides of the cell membrane, (2) absorption of the potassium into the cell membrane, or (3) penetration of excess of potassium into the cell. Similarly, the effect of magnesium and its interrelationships with potassium remain to be investigated. The profound effects of these ions on myosin adenosinetriphosphatase and on the contraction of isolated myofibrils are well known.[17]

Another important question concerns the nature and type of metabolic activity maintained by the seemingly inactive heart. There is insufficient anoxia to cause demonstrable damage on the electrocardiogram or myogram when the beat returns after perfusion. In unpublished studies, we have regularly kept the intact dog's heart in standstill for 45 minutes, followed by return of the heart to normal and survival in 80% of the dogs.

Summary

The isolated perfused cat heart system has been found to be a simple and practical method for evaluating and designing cardioplegic solutions for use in intracardiac surgery. Using this method, it was found that potassium citrate and magnesium sulfate have synergistic properties and are more efficient in combination than when used

alone. The addition of neostigmine to the mixture did not interfere with the return of the heart beat but did allow a slow rate in the immediate washout period.

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REFERENCES

1. Ringer, S. J.: A Further Contribution Regarding the Influence of the Different Constituents of the Blood on the Contraction of the Heart, J. Physiol. 4:29, 1883.

2. Hooker, D. R.: On the Recovery of the Heart in Electric Shock, Am. J. Physiol. 91:305, 1929.

3. Wiggers, C. J.: Studies on Ventricular Fibrillation Produced by Electric Shock: III. The Action of Antagonistic Salts, Am. J. Physiol. 93: 197, 1930.

4. Swan, H., and Zeavin, I.: Cessation of Circulation in General Hypothermia: III. Technics of Intracardiac Surgery Under Direct Vision, Ann. Surg. 139:385, 1954.

5. Senning, A.: Ventricular Fibrillation During Extracorporeal Circulation, Acta chir. scandinav., Supp. 171, 1952.

6. Lam, C. R.; Geoghegan, T., and Lepore, A.: Induced Cardiac Arrest for Intracardiac Procedures: An Experimental Study, J. Thoracic Surg. 30:620, 1955.

7. Melrose, D. G.; Dreyer, B.; Bentall, H. H., and Baker, J. B. E.: Elective Cardiac Arrest, Lancet 2:21, 1955.

8. Effler, D. B.; Groves, L. K.; Sones, F. M., Jr., and Kolff, W. J.: Elective Cardiac Arrest in Open Heart Surgery: Report of 3 Cases, Cleveland Clin. Quart. 23:105, 1956.

9. Moulder, P. V.; Thompson, R. G.; Smith, C. A.; Siegel, B. L., and Adams, W. E.: Cardiac Surgery with Hypothermia and Acetylcholine Arrest, J. Thoracic Surg. 32:360, 1956.

10. Young, W. G., Jr.; Sealy, W. C.; Brown, I. W., Jr.; Hewitt, W. C., Jr.; Callaway, H. A., Jr.; Merritt, D. H., and Harris, J. S.: A Method for Controlled Cardiac Arrest as an Adjunct to Open Heart Surgery, J. Thoracic Surg. 32:604, 1956.

11. Montgomery, A. V.; Prevedel, A. E., and Swan, H.: Prostigmine Inhibition of Ventricular Fibrillation in the Hypothermic Dog, Circulation 10:721, 1954.

12. Chenoweth, M. B., and Koelle, E. S.: An Isolated Perfusion System Adapted to the Determination of Non-Gaseous Metabolites, J. Lab. & Clin. Med. 31:600, 1946.

13. Langendorff, O.: Untersuchungen am überlebenden Säugethierherzen, Arch. Physiol. 61:291, 1895.

14. Lam, C. R., in discussion on Moulder,[9] p. 371.

15. Moulder, P. V., and Thompson, R. G.: Protection of the Heart Under Hypothermia with Acetylcholine Arrest, Proc. Soc. Exper. Biol. & Med. 92:49, 1956.

16. DiPalma, J. R., and Schults, J. E.: Antifibrillatory Drugs, Medicine 29:123, 1950.

17. Engbaek, L.: The Pharmacological Actions of Magnesium Ions with Particular Reference to the Neuromuscular and the Cardiovascular Systems, Pharmacol. Rev. 4:396, 1952.

Reconstruction of the Amputated Thumb

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Introduction

Amputation of the thumb is not a common injury. Over a period of five years, from Jan. 1, 1952, to Dec. 31, 1956, we have had 15 cases of thumb amputation in the Arabian American Oil Company hospitals. These cases occurred among 581 hospital admissions for injuries to the hand, not including the many more cases treated in the outpatient department. As compared with amputations of the rest of the fingers, the thumb amputations comprise 13.7%, a total of 109 traumatic finger amputations having been seen in 70 patients. The thumb injuries, in general, numbered 61 cases, or 10% of the total injuries for which patients were admitted. Of the 15 cases of amputated thumb, 3 only were serious enough to require reconstructive surgery, that is, 0.5% of the total admissions for hand injuries (Table). The rest of the injuries were at a more distal level.

This small number of thumb amputations requiring reconstructive surgery, namely, 0.5%, or 3 cases among 581 admissions during five years in such a busy industrial center as Aramco, and actually only one case, that of an industrial injury in an employee, whereas the other two were of nonindustrial injuries in nonemployees, points up the fact that only a very few surgeons have adequate experience in the problem of reconstructive surgery of the amputated thumb.

Submitted for publication May 2, 1957.

From the Department of Surgery, Dhahran Health Center.

Thumb and Finger Amputations in Arabian American Oil Company

	No. of Patients	Percentage
Total cases of hand injuries admitted	581	100
Total thumb injuries	61	10.5
Total cases of finger amputations, including the thumb	70	12
Total fingers amputated in the 70 patients	109	
Thumb amputations	15	13.7% of the total no. fingers amputated and 2.5% of the total no. of admissions
Thumb amputations that required reconstruction	3	0.5% of all the hand injuries admitted

The importance of the thumb for the pincer action cannot be overestimated. The loss of a thumb is a great disability to any member of the community. The magnitude of the disability led many hand surgeons to devise a multitude of reconstructive procedures, from the simplest to the most intricate, such as the transplantation of a toe to the hand for replacing an amputated thumb.

A few points about the anatomy of the thumb are worthy of mention.

Insertion of Opponens Pollicis Muscle.—This muscle, as well as the rest of the thenar muscles, may be very powerful. The opponens arises from the greater multangular bone and the transverse carpal ligament and is inserted into the whole length of the first metacarpal bone on its radial side.

Other Small Muscles of Thumb.—These are inserted into the base of the proximal phalanx. When the thumb is amputated at the metacarpophalangeal joint, or even through the distal half of the metacarpal, the power of opposition is not lost because of the spared insertion of the opponens. The other small muscles also reattach themselves and contribute to the movements of the stump.

Long Flexor and Two Extensor Pollicis Muscles.—These muscles are put out of action in all amputations proximal to the base of the proximal phalanx because of

their insertions into the bases of the phalanges of the thumb.

Abductor Pollicis Longus Muscle.—This muscle is inserted into the base of the metacarpal and takes care of abduction and some extension of the reconstructed thumb, while the small muscles of the thumb take care of the flexion and adduction.

Comment: This short survey explains the very good function that follows the reconstruction of a thumb by the procedure to be described with all or part of the metacarpal spared. In these cases one does not have to worry about tendon reconstruction.

The cases reported reveal the rapidity with which the reconstructed thumb is reinnervated. This fact and the good function acquired after reconstruction of the amputated thumb led me to favor the lengthening of the amputated thumb by tubular skin graft and a bone graft rather than by one of the other methods to be mentioned.

Sites of Amputations and Possible Corrective Procedures.—1. At Middle of Proximal Phalanx or Anywhere Distal to This Level: In these cases the amount of disability is not great enough to justify reconstructive surgery. On the other hand, a prosthesis may be used for cosmetic purposes.

2. Proximal to Middle of Proximal Phalanx with Part of Metacarpal Left: The reconstruction of the thumb in these cases by one of the methods described in the literature is worthy of consideration. The possible methods are (*a*) deepening the cleft between the thumb and the hand; (*b*) lengthening the thumb by tubular skin and bone grafts; (*c*) pollicization of an index or a middle finger; (*d*) pollicization of a toe.

3. At the Carpometarcarpal Joint: Here the problem is serious because a thumb so built up is going to be practically devoid of movement; moreover, there is no good anchorage available for the bone graft.

Pollicization of another finger, or a toe, is technically a difficult procedure; moreover, only a very few people are confident of a good result following such a venture. In the third case reported in this paper, reconstructing a thumb by building it with tubular skin and bone provided position but no movement of opposition. The fixing of the bone graft into the carpal bone in a position of opposition furnished a base for the other fingers on which to perform the pincer action. The result obtained in this case justified the operation.

Operative Procedures

Stage 1.—Two parallel incisions are made in an appropriate region of the abdomen so that when the hand is attached to the tube no strain will be thrown on any joints of the upper extremity. The flap made is of the desirable size to reconstruct a thumb, usually 4×10 cm. The flap is elevated and sutured back in place. The flap includes the fatty layer of the superficial abdominal fascia. This stage can be omitted, but I found that when the tube is made in two stages, less edema of the tube develops. This stage may be done with use of local anesthesia.

Stage 2.—After six to seven days the sutures are removed and the skin flap is tubed; very fine needles and silk are used—0000 or 00000 nonabsorbable surgical (silk) sutures. The sutures should not be tight and should be placed near the edge of the skin.

After about 10 days the blood supply to the tube is directed to come more from the direction to be interrupted last. A rubber band is tied around the end of the tube to be interrupted first (Fig. 1). The rubber band is left for 10 minutes the first day, and the time is progressively increased about 10 minutes daily. The band causes discomfort, but the patient can stand it with some encouragement and explanation.

The site of the tube may be covered with split-thickness skin, as in the last two cases, or by closure of the widely undermined skin, as in the first case (Fig. 2).

The patient is always more comfortable postoperatively if the donor area in the

Figure 1

Figure 2

abdomen is covered with split-thickness skin rather than by approximation of the undermined skin (Fig. 3).

Stage 3.—This stage is started three weeks after the tubing and, like the second stage, is done under general anesthesia. The tube is interrupted at the appropriately chosen and conditioned end. The abdominal wound is repaired. The recipient site is prepared by excising an area of skin, including the scar over the thumb or wrist, to leave a defect slightly larger than the apparent size of the cross section of the tube, because the tubed skin is contracted and can take some stretching. Too much stretching, too many and too tight sutures, are not desirable.

The tubed graft is transferred to the hand. The sutures are removed on the 10th day, when the development of the graft is commenced, as in Stage 2 (Fig. 4).

I use padding and Elastoplast to fix the extremity, and not plaster of Paris. The wounds are inspected frequently; any hematoma or infection should be spotted and drained promptly.

This stage is a very important one, and a minimum of four weeks should be allowed to ensure success.

Stage 4.—Four weeks later, with local anesthesia, the tube is detached from the abdomen. The abdominal wound is repaired; so is the wound in the tube. To have a good-looking stump, the edges of the tube are excised and two equal flaps fashioned with curved edges so as to have an end that looks like a thumb.

The anesthesia is needed only to block the nerves in the abdomen. The anesthetic agent is not to be injected into the tube.

The flaccid reconstructed thumb is supported with a splint to avoid kinking (Fig. 5). The bandages and dressings should be very loose, so as not to hamper the very important growing blood supply. The sutures are left for 10 days. If the end of

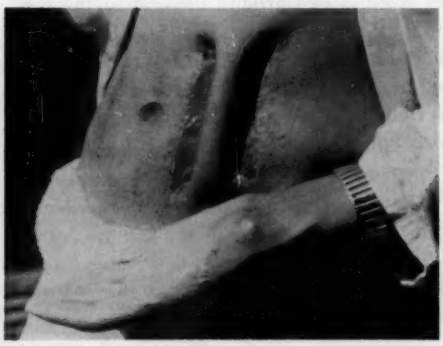

Figure 3

Figure 4

Figure 5

the tube becomes necrotic, it should be revised, without anesthesia, at an early date.

Stage 5.—About two weeks later the tube is supported with a bone graft. I prefer a segment from the seventh rib excised where the rib has the maximum curve, which is near the midaxillary line. This slight curve will give the reconstructed thumb a desirable position of little flexion. Figure 6A and 6B demonstrates this fact and the degree of opposition.

The rib is exposed in the usual manner up to the periosteum; this is not stripped as usual. I excise the rib segment with its outer periosteum intact; this encourages the viability of the graft from the start. The osteoblasts in the periosteum will continue their function, and the graft does not have to depend on creeping substitution only to live, unite, and function.

Excision and fashioning of the rib require particular attention. Parallel incisions are made in the periosteum near each border of the rib (Fig. *7A*). The periosteum is stripped around the edges, leaving the part between the incisions in situ (Fig. *7B*). The rib segment, of the desirable length, is excised with its outer periosteum intact (Fig. *7C*) and the wound in the chest wall repaired.

The bone is fashioned by excising the two borders devoid of periosteum. This step, I believe, will encourage revascularization of the bone because it exposes cancellous bone. Only enough border should be excised with either an osteotome or an electric saw (Fig. *7D*). Removal of too much bone will weaken the graft and may result in separation of the two plates of compact bone and destroy the graft. Then follows the next step, where precision is essential. The graft is trimmed to measure; the length of the graft should be equal to the length of the skin tube plus the length of the medullary canal of whatever bone is going to be used for impaling the rib as far as it can go. This part of the rib has to be trimmed narrower than the rest. Attention is now directed to the tubular graft; this is split at the site of the old scar, preferably by excising the scar down to the center of the tube from the original stump to within 1 cm. of the distal end. A little scar tissue is excised from the center of the tube and over the bone end to be used for anchoring the rib graft. The medullary canal of the metacarpal is prepared to receive the rib by tunneling it with an awl or a similar instrument. If one of the carpal bones is used, a tunnel is prepared in this bone with

Figure 6A

Figure 6B

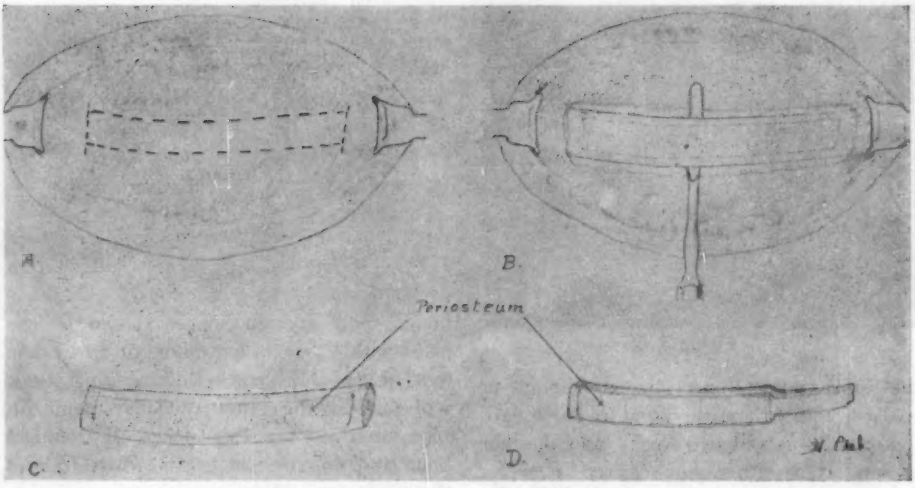

Fig. 7.—Diagrams showing stages in excising and fashioning a rib segment with periosteum of the bone graft.

a similar instrument of favorable size. The length of the tunnel in the receiving bone used is measured and the rib end to be impaled into it is trimmed to appropriate thickness for the distance that is to be buried only (Fig. 7*D*). The periosteum over the part to be buried is excised. If there is cartilage over a metacarpal, this is removed. The rib should fit snugly into the receiving bone. Precision is most important here. This will reduce the necessity of rigid immobilization, and the patient can exercise the thenar muscles from the start.

The rib is fixed in such a way that its gentle concavity will face the rest of the fingers when in opposition (Fig. 8). The tubular graft is sutured over the rib. Hemostasis is important. Frequent inspection to spot infection or hematomas for prompt drainage is justifiable. Figure 9 shows the last stage with the sutures in situ and the pincer action regained.

External splinting with splints or plaster is desirable for two to four months. The average length of time for these five procedures is about 10 weeks. The patient does not have to be hospitalized all through this period.

The growth of sensory nerves into the reconstructed thumb and the development of sensory power seem to follow the rate of 1 mm. in two days. The reconstructed thumb acts as a thumb, with ankylosis of the interphalangeal and metacarpophalangeal

Figure 8

Figure 9

joints. The function regained is worth the multiple procedures and the hospitalization period.

The following are the three cases in which reconstructive surgery was needed in the five-year period.

Report of Cases

CASE 1.—Saudi Arab boy; aged 12. This patient had a snake bite on his right thumb on Sept. 15, 1954; he was treated elsewhere by tourniquet and incision over the metacarpophalangeal joint. He was admitted to this hospital on Sept. 16. There was uncontrollable infection and gangrene, which led to amputation of the thumb at the neck of the metacarpal bone. The wound healed well, and reconstruction of the right thumb was started.

Stage 1.—On Oct. 2, with local anesthesia, a skin flap was elevated from the right side of the abdomen and sutured back in place.

Stage 2.—On Oct. 9, the skin flap was tubed and the defect closed by undermining the skin.

Stage 3.—On Oct. 31, that is, about three weeks later, the tube was attached to the hand.

In Stages 2 and 3 development of the graft blood supply was directed by tying a rubber band at the end to be interrupted first.

Stage 4.—On Nov. 28, that is, four weeks later, the tubed graft was interrupted from the abdomen, under local anesthesia.

Stage 5.—On Dec. 11, that is, about two weeks later, the rib graft was applied.

The patient was discharged on Dec. 30. By then he had sensation in the proximal 2 cm. of the graft only. A cast was reapplied, and the patient was asked to report back after four weeks. This was the last we heard of him.

CASE 2.—A Saudi Arab man, carpenter; age 29.

This patient sustained an injury to his left hand from a machinery accident on June 24, 1956. The accident resulted in traumatic amputation of the left thumb and avulsion of skin and subcutaneous tissues over the distal phalanx of the left index finger. The amputated thumb was revised at the metacarpophalangeal joint and the index finger avulsion covered with a pedicled skin graft, which took well.

The patient was referred to me for reconstruction of his left thumb.

Stage 1.—On July 7, a skin flap was elevated from the left side of the abdomen and sutured back in place under local anesthesia.

Stage 2.—On July 15, the skin flap was tubed and the defect covered with split-thickness skin.

Stage 3.—On Aug. 4, that is, three weeks later, the tubed graft was transferred to the stump of the amputated thumb and the cartilage over the metacarpal head excised.

During Stages 2 and 3 development of the blood supply of the graft was directed by tying a rubber band around the end to be interrupted.

Stage 4.—On Sept. 2, that is, four weeks later, the graft was detached from the abdomen under local anesthesia.

Stage 5.—On Sept. 16, that is, about two weeks later, and after the wounds healed well, a rib segment was fixed into the graft. The thumb was immobilized with a splint for about three months, allowing some movements at the carpometacarpal joint to exercise the thenar muscles, and the patient was allowed to begin light duties.

From the beginning, the patient had good range of motion; he could appose the thumb to the little finger.

At four months, the bone united well, and sensation was acquired all over the graft. Movements were excellent and the power of opposition very good. The patient was released to full duties as a carpenter.

CASE 3.—Saudi Arab schoolboy; age 16.

This boy sustained an accidental gunshot wound of his left hand on April 8, 1956, which resulted in the loss of the thumb, including the thenar eminence through the carpometacarpal joint. A small part of the greater multangular bone was lost also. Other injuries were partial amputations of the left middle and ring fingers through the distal phalanges. He was admitted to the hospital and his wounds revised. The patient was discharged on April 21, with healed wounds and complete loss of the left thumb, including all the thenar eminence through the greater multangular.

On July 22, the patient was referred to me and was admitted to the hospital for reconstruction of a left thumb.

Stage 1.—On July 23, a skin flap was elevated from the left side of the abdomen under local anesthesia.

Stage 2.—On July 29, the graft was tubed and the site covered with split-thickness skin.

Stage 3.—On Aug. 18, that is, three weeks later, the tube was transferred to a raw area at the lateral aspect of the left wrist produced by excising an oval piece of skin over the greater multangular bone. On Sept. 8, the patient was discharged for bad behavior, with his hand attached to his abdomen by the tubed graft. He was a source of entertainment in his town for a few days.

During Stages 2 and 3 the blood supply of the graft was directed by tying a rubber band around the end to be interrupted. The patient was readmitted on Sept. 9, 1956, for further surgery.

Stage 4.—On Sept. 12, that is, less than four weeks later, the tube was detached from the abdomen under local anesthesia and the wounds repaired. The patient was again discharged, after

his wounds had healed, on Sept. 24. He was readmitted on Sept. 29.

Stage 5.—On Oct. 1, that is, about three weeks after Stage 4, the rib graft was applied. The bone graft was introduced into the greater multangular bone through a large drill hole, and a plaster-of-Paris cast was applied. The wounds healed. The patient was discharged on Oct. 9, with a new cast. He was followed up in the outpatient department at three-week intervals, where the cast was changed and x-rays taken. On Jan. 28, that is, about four months after the rib graft, the x-ray showed good bone union. At this time sensation was acquired in all the graft. The patient as well had about 5 degrees of motion in his reconstructed thumb. I could not explain how this movement at the carpal joint was produced.

All along the patient was practicing the pincer action. As his thumb had small anchorage into the greater multangular bone, and this was not very secure, he was asked to report for a reconstruction of a web between the thumb and the palm of the hand. He agreed to be readmitted during the school summer vacation.

Summary

The pincer action can be restored to the hand with an amputated thumb through several procedures mentioned above. I prefer lengthening of the thumb. A detailed outline of the operation is given, and three cases are presented.

Dr. Robert Clinton Page, Medical Director, and Dr. H. Lohnaas, Chief Surgeon, made the publication of this paper possible. Miss H. Beam, our secretary, gave assistance in its preparation. Miss H. Ptak made the diagrams. Miss A. Lysczyk, our Medical Records librarian, provided statistical records.

Arabian American Oil Company.

REFERENCES

1. Bunnell, S.: Surgery of the Hand, Ed. 2, Philadelphia, J. B. Lippincott Company, 1950.

2. Cross, C. M., Editor: Gray's Anatomy of the Human Body, Ed. 26, Philadelphia, Lea & Febiger, 1954.

3. Kaplan, E. B.: Functional and Surgical Anatomy of the Hand, Philadelphia, J. B. Lippincott Company, 1953.

4. Rank, B. K., and Wakefield, A. R.: Surgery of Repair as Applied to Hand Injuries, Baltimore, Williams & Wilkins Company, 1953.

Prevention of Nonhemolytic Blood Transfusion Reactions with an Antihistamine, Chlorpheniramine

Report of 6131 Cases

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Approximately 4,000,000 blood transfusions are given annually in the United States.[1] This widespread use of fresh and stored whole blood has focused increasing attention on the prevention and treatment of transfusion reactions.

Pyrogenic reactions occur most frequently [2-7] and are characterized by chills, fever, vomiting, nausea, and, in severe cases, prostration. They are caused by exogenous pyrogens introduced by the donor's blood or by contaminated transfusion equipment.[8]

Allergic reactions, next in frequency, include urticaria, angioneurotic edema, dyspnea, asthma, and, occasionally, anaphylactic shock. They are caused by the release of histamine to its receptor site in the cells. This has been confirmed by Muñoz-Baratta,[9] who was able to produce the allergic type of transfusion reactions by injections of histamine. Winter and Taplin [10,11] believe that allergic reactions to transfusion are 10 times as frequent among patients with a history of allergy; however, in earlier experiments, De Gowin and Hardin [12,13] failed to establish a correlation between a history of asthma and greater likelihood of allergic response to transfusion.

Other types of reactions, although more serious, are comparatively rare. Serum hepatitis, a grave and sometimes fatal complication, can be prevented by careful screening of donors and elimination of those with a positive history of jaundice. Cardiac arrest is sometimes precipitated by circulatory overload, especially in patients with diminished cardiac function who receive blood too rapidly or in amounts which exceed circulatory tolerance. Hemolytic reactions, most dangerous of all, are caused by administration of mismatched blood. Improved techniques of typing, cross matching, and handling blood for transfusion will reduce their incidence.

De Gowin and Hardin [12,13] have shown that all types of reactions occur after the administration of either fresh or stored blood and that, when stored blood is used, neither the age of the blood nor the preservative affects the type of incidence of transfusion reactions. However, the conditions under which blood is collected, stored, and administered influence the reaction rate; hospitals with superior equipment and personnel have substantially fewer instances of all types of transfusion reactions.[14,15]

Numerous reports [10,11,14-34] cite the use of antihistamines to prevent allergic and pyrogenic transfusion reactions. The action of antihistamine in overcoming allergic reactions derives from its ability to prevent the access of histamine to its receptor site in the cell.[35]

Although Wilhelm [32,33] and Winter and Taplin [10,11] do not believe that antihistamines are useful in preventing pyrogenic reactions, the general experience has been that these agents can reduce pyrogenic, as well as allergic, reactions.[14,16,20-22,27,29,30] The mechanism by which antihistamines are able to prevent pyrogenic reactions is not clearly understood. A possible explanation is offered by Ferris [20,21] and Stephen,[30] who sug-

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TABLE 1.—*Reactions in Cases Not Treated with Antihistamines*

Investigator	No. of Transfusions	Pyrogenic	Per Cent Pyrogenic	Allergic	Per Cent Allergic	Hemolytic	Per Cent Hemolytic	Miscellaneous	Per Cent Miscellaneous
Lundy and others[9]	7,957	188	2.36	201	2.52	1	0.01	28	0.35
Seldon[6]	8,222	170	2.1	106	1.3	0	0	42	0.5
Winter & Taplin[10]	264	18	6.8	12	4.5				
De Gowin & Hardin[11]	1,604	61	3.8	24	1.49	5	0.31	9	0.56
Arrau & Giacaman[14]	195	49	25.1	17	8.7			11	5.6
Alfonsi[16]	383	53	15.0	15	3.9				
Ferris and others[21]	742	32	4.31	21	2.82	0	0	1	0.16
Hoffmann[28]	109 *			13	12.0				
Simon & Eckman[20]	995	8	0.8	10	1.0				
Stephen and others[30]	2,636	89	3.3	47	1.7	2	0.07		
Wilhelm and others[33]	453	9	1.71	5	1.01	0	0		
This study	3,346	100	3.01	47	1.40	1	0.03	21 †	0.60
Summary, all investigators	26,906	777	2.89	518	1.92	9	0.03	112	0.42

* All to known allergic reactors.
† Combined allergic and pyrogenic reactions.

gest that pyrogenic response to transfusions may be on an allergic basis.

Laboratory studies indicate that adding an antihistamine to whole blood does not alter the constituents of the blood, and Wilhelm's [32,33] in vitro experiments showed that antihistamines do not cause increased hemolysis in whole stored blood. This has been confirmed clinically by the fact that hemolytic reactions occur with equal frequency after transfusions with and without antihistamine and, therefore, are neither masked nor produced by antihistamines.[20,30]

Drowsiness occasionally follows administration of antihistamine in transfused blood. However, most investigators [14,15,25,36,37] do not consider this undesirable, since nearly all patients who require transfusions are bedfast and very ill.

The antihistamines have been administered orally on the day before transfusion and parenterally immediately before transfusion, but experience has shown that the most effective method is addition of the antihistamine to the blood immediately prior to use.[9,10,11,14]

TABLE 2.—*Reactions in Cases Treated with Antihistamines*

Investigator	No. of Transfusions	Pyrogenic	Per Cent Pyrogenic	Allergic	Per Cent Allergic	Hemolytic	Per Cent Hemolytic	Miscellaneous	Per Cent Miscellaneous	Drug and Dose
Winter & Taplin[10]	664	42	6.32	5	0.75					Chlorpheniramine maleate: 10 mg.
Arrau & Giacaman[14]	130	1	0.8	0	0			0	0	Chlorpheniramine maleate: 10 mg.
Alfonsi[16]	350	14	4.0	0	0					Antazoline hydrochloride: 200 mg.
Bernhard and others[17]	1004	14	1.39	11	1.09	0	0			Methapyrilene hydrochloride: 10 mg.
Ferris and others[21]	607	0	0	1	0.16	1	0.16	0	0	Tripelennamine hydrochloride, 25 mg.
Hoffmann[28]	108 *			0	0					Chlorpheniramine maleate: 10 mg.
Pellegrino & Oliveira[27]	289	7	2.42	0	0					Chlorpheniramine maleate: 10 mg.
Simon & Eckman[20]	987	2	0.21	0	0					Chlorpheniramine maleate: 10 mg.
Stephen and others[30]	2570	55	2.1	11	0.3	1	0.03			Tripelennamine citrate: 25 mg.
Wilhelm and others[33]	495	11	2.22	0	0	1	0.20			Diphenhydramine hydrochloride: 50 mg.
This study	2785	15	0.54	2	0.07	1	0.03	1 †	0.03	Chlorpheniramine maleate: 10 mg.
Summary, all investigators	9989	161	1.61	30	0.30	4	0.04	1	0.01	-- -- --

* All to known allergic reactors.
† Combined allergic and pyrogenic reactions.

Antihistamines are sometimes used therapeutically for blood transfusion reactions, but results are much more favorable when the agents are used prophylactically.[20,28,30]

A comparison of the reaction rates with and without concurrent antihistamine administration is presented in Tables 1 and 2. In a total of 26,906 transfusions, without an antihistamine, there were 777 pyrogenic reactions (2.89%) and 518 allergic reactions (1.92%). In 9989 transfusions with an antihistamine, there were 161 pyrogenic reactions (1.61%) and 30 allergic reactions (0.30%).

These favorable reports, and the promising results which we had obtained previously in a small series,[38] stimulated more extensive study.

Method

We selected chlorpheniramine maleate (Chlor-Trimeton*) because it is the most potent of the antihistamines, produces the fewest side-effects, and acts rapidly after parenteral administration. Also, it offers high concentration in a minimal volume of solution.

We confirmed its compatibility with whole blood in the following manner: Eight pints (4000 cc.) of blood were drawn into vacuum flasks containing 120 ml. anticoagulant acid citrate dextrose solution U. S. P. Four of the flasks were inoculated with 20 mg. of chlorpheniramine maleate and one with 50 mg. of chlorpheniramine maleate. The remaining three flasks served as controls.

All flasks were stored under blood-bank conditions for 21 days, and samples, taken under complete asepsis, were examined for color and appearance at 48-hour intervals. Complete hemogram, prothrombin time, and sedimentation rate determinations revealed no significant differences between the control and the treated flasks of blood.

We recorded all reactions in a series of 6131 blood transfusions. Of these, 3346 were given without the antihistamine and 2785 received the antihistamine in the following manner: Ten milligrams of chlorpheniramine maleate was withdrawn into a sterile syringe from the 1 cc. ampuls. The diaphragm of the blood flask was sterilized; the antihistamine was injected just prior to transfusion; the flask was rotated gently for even distribution, and the transfusion was given in the usual manner. The treated and untreated transfusions were administered at random to the patients in this series without regard for such factors as age, sex, or diagnosis. If multiple transfusions were required, 10 mg. of chlorpheniramine maleate was added once every six hours.

* The Chlor-Trimeton maleate used in this study was supplied by the Clinical Research Division of the Schering Corporation, Bloomfield, N. J.

Results

In the control series, of 3346 cases, there were 47 allergic reactions, 100 pyrogenic reactions, 21 combined allergic and pyrogenic reactions, and 1 hemolytic reaction.

Among the 2785 cases in which the antihistamine was added, there were 2 allergic reactions, 15 pyrogenic reactions, 1 instance of a combined reaction, and 1 hemolytic reaction.

The incidence of allergic reactions was thus reduced from 1.40% to 0.07% by the addition of the antihistamine. Pyrogenic reactions were similarly reduced from 3.01% to 0.54% and the incidence of combined reactions was reduced from 0.60% to 0.03%. The antihistamine did not alter the incidence of hemolytic reactions, which was 0.03% in both groups.

There were no undesirable sequelae attributable to the antihistamine. Drowsiness was observed occasionally, but we agree with other investigators that this is no disadvantage among patients who receive blood transfusions.

The following case reports are typical of those in our series.

CASE 1.—A woman aged 27 received 8 units of blood over a three-year period for episodes of metrorrhagia and incomplete abortion. Each transfusion was followed by urticaria, pyrexia, chills, and respiratory discomfort, singly or in combination. When chlorpheniramine was added to two subsequent transfusions, there were no reactions. A later transfusion, again without the antihistamine, was followed by urticaria and chills.

CASE 2.—A man aged 70, with chronic lymphatic leukemia, received 3 units of blood after oral administration of an antihistamine. There were two instances of urticaria and one of chills. Chlorpheniramine was administered intravenously with 15 subsequent transfusions. After four of these transfusions, there were mild prodromal symptoms, indicating a possible reaction, and an additional 10 mg. of the antihistamine was given. Only one of these episodes developed into a reaction, consisting of chills without urticaria.

CASE 3.—A man of 45 with heavy-metal intoxication of the marrow, received 250 units of blood over a period of five years. Chills and urticaria almost invariably followed the 242 units which were given without chlorpheniramine. Oral antihistamines were ineffective. The final 8 units of blood were given with chlorpheniramine. There was no urticaria, and only two instances of slight or moderate chills.

Comment

Some investigators feel that antihistamines should be administered prophylactically only to patients with a history of allergy; others advocate routine use in all transfusions. On the basis of our results, we recommend routine addition of an antihistamine to flasks of blood before transfusion. It is a safe, simple, and extremely efficacious procedure. Also, the emergency nature of many transfusions may preclude prior establishment of an allergic history.

Previously, we had attempted to prevent allergic and pyrogenic reactions by administering the antihistamine orally or subcutaneously before transfusion, but the results were inconclusive. We found, however, that direct introduction of the antihistamine into the flask of blood immediately before transfusion provided the safety, ease of administration, and consistently favorable results which we sought.

Summary

Chlorpheniramine maleate (Chlor-Trimeton maleate) is compatible with whole blood. It produces no detectable alterations in either fresh or stored blood.

No untoward reactions attributable to the antihistamine occurred in the 2785 patients who received it during transfusion.

The incidence of nonhemolytic transfusion reactions was markedly reduced by the addition of 10 mg. of chlorpheniramine maleate. Allergic reactions were reduced from 1.40% to 0.07%; pyrogenic reactions were reduced from 3.01% to 0.54%, and combined allergic and pyrogenic reactions were reduced from 0.60% to 0.03%. The incidence of hemolytic reactions was 0.03% in both groups.

Since our results show that adding 10 mg. chlorpheniramine to whole blood reduces allergic and pyrogenic reactions substantially, we recommend this as a routine procedure.

19 Holly St., Cranford, N. J.

REFERENCES

1. Vogel, P.: Current Problems in Blood Transfusion, Bull. New York Acad. Med. 30:657-674 (Sept.) 1954.

2. Lundy, J. S., and others: Annual Report for 1951 of Section of Anesthesiology, Including Data and Remarks Concerning Blood Transfusion and the Use of Plasma Substitutes, Proc. Staff Meet. Mayo Clin. 27:512-526 (Dec. 3) 1952.

3. Rath, C. E.: Practical Therapeutics: Hazards of Blood Transfusions, GP 7:67-74 (June) 1953.

4. Schattenberg, H. J., and Noxon, G. K.: Reactions and Complications Following Transfusion, Texas J. Med. 47:27-32 (January) 1951.

5. Scudder, J.: Transfusion Reactions During 12 Years of Banked Blood at the Presbyterian Hospital, New York J. Med. 53:538-539 (March 1) 1953.

6. Seldon, T. H.: Management of Blood Transfusion Reactions, M. Clin. North America 40: 1217-1224 (July) 1956.

7. Straus, B., and Torres, J. M.: Use and Abuse of Blood Transfusion, J. A. M. A. 151:699-701 (Feb. 28) 1953.

8. Hargraves, M. M.: Transfusion Reactions and Their Treatment, M. Clin. North America 31: 803-805 (July) 1947.

9. Muñoz-Baratta, C.: La prevención y tratamiento de la reacciones post-transfusionales no hemolíticas con el uso de los antihistamínicos, Rev. san. polic. 12:198 (Nov.-Dec.) 1952.

10. Winter, C. C., and Taplin, G. V.: The Value of Chlor-Trimeton [R] in the Management of Acute Allergic and Febrile Reactions to Blood Transfusions, Ann. Allergy 12:717-727 (Nov.-Dec.) 1954.

11. Winter, C. C., and Taplin, G. V.: Prevention of Acute Allergic and Febrile Reactions to Blood Transfusions by Prophylactic Use of an Antihistamine Plus an Antipyretic, Ann. Allergy 14: 76-81 (Jan.-Feb.) 1956.

12. De Gowin, E. L., and Hardin, R. C.: Studies on Preserved Human Blood: Reactions from Transfusion, J. A. M. A. 115:895-899 (Sept. 14) 1940.

13. De Gowin, E. L., and Hardin, R. C.: Reactions from the Transfusion of Preserved Blood, Brit. M. J. 2:1-5 (July 6) 1940.

14. Arrau, C. M., and Giacaman, S.: Prevention of Nonhemolytic Posttranfusional Reactions with Antihistaminics, personal communication to the authors, 1953.

15. Muñoz-Baratta, C.: Prevención de las reacciones transfusionales no hemolíticas agregando un antihistamínico dentro del frasco de sangre, momentos antes de transfundirla, Rev. san. polic. 13: 159 (March-April) 1953.

16. Alfonsi, P. L.: Il trattamento di alcune reazioni trasfuzionali con antistaminico, Gazz. med. ital. 111:71-73 (March) 1952.

17. Bernhard, W. G.; Grubin, H., and Bryan, M. V.: Prophylactic Use of an Antihistamine in Blood Transfusions, J. M. Soc. New Jersey 50: 542-545 (Dec.) 1953.

18. Blumenthal, L. S., and Rosenberg, M. H.: Diphenhydramine Hydrochloride ("Benadryl Hydrochloride"): Report on Its Use in 137 Patients, J. A. M. A. 135:20-25 (Sept. 6) 1947.

19. Davenport, J. W., Jr.: Transfusion Reactions and Their Treatment, Am. J. Clin. Path. 24:331-338 (March) 1954.

20. Ferris, H. E.; Alpert, S., and Coakley, C. S.: Prevention of Allergic Transfusion Reactions: Prophylactic Use of Antihistamines in Blood to Prevent Allergic Transfusion Reactions, Am. Pract. & Digest. Treat. 3:177-183 (March) 1952.

21. Ferris, H. E.; Alpert, S., and Coakley, C. S.: Transfusion Reactions, New York J. Med. 53: 539 (March 1) 1953.

22. Frankel, D. B.: Use of Chlorprophenpyridamine Maleate Injection in Blood Transfusion, Ann. Allergy 13:319 (May-June) 1955.

23. Frankel, D. B., and Weidner, N.: Use of Chlor-Trimeton Maleate Injectable in Blood Transfusions, Ann. Allergy 11:204-205 (March-April) 1953.

24. Hampton, A. G., Jr., and others: Dangers of Blood Transfusions, Virginia M. Month. 82: 217 (May) 1955.

25. Hoffmann, C. R.: Allergic Reactions to Blood Transfusion: Their Prevention with Injectable Chlor-Trimeton, personal communication to the authors, 1954.

26. Krevans, J. R.: Hazards of Blood Transfusion, Postgrad. Med. 19:41-44 (Jan.) 1956.

27. Pellegrino, V., and Oliveira, G. J. A.: Use of Antihistamines as Prophylactic Measures in Post-Transfusion Reactions of Allergic and Pyrogenic Types, read at the Second International Congress of Allergology, Rio de Janeiro, Brazil, November, 1955.

28. Seldon, T. H.: Reactions to Transfusions During an Operation, S. Clin. North America 29: 1129-1135 (Aug.) 1949.

29. Simon, S. W., and Eckman, W. G., Jr.: The Use of Chlor-Trimeton in Prevention of Blood Transfusion Reactions, Ann. Allergy 12:182-184 (March-April) 1954.

30. Stephen, C. R., and others: Antihistaminic Drugs in Treatment of Nonhemolytic Transfusion Reactions, J. A. M. A. 158:525-529 (June 18) 1955.

31. Triantaphyllides, G., and Athitakis, C.: Une nouvelle méthode relative à la transfusion sanguine, Gaz. méd. France 61:289-292 (Feb.) 1954.

32. Wilhelm, R. E., and others: The Value of Antihistaminics in the Prevention of Blood Transfusion Reactions, J. Michigan M. Soc. 53:651, (June) 1954.

33. Wilhelm, R. E., and others: Antihistamines for Allergic and Pyrogenic Transfusion Reactions, J. A. M. A. 158:529-531 (June 18) 1955.

34. Young, L. E.: Some Newer Aspects of Blood Transfusion Therapy, Mississippi Doctor 30:204-207 (Dec.) 1952.

35. Goodman, L. S., and Gilman, A.: The Pharmacological Basis of Therapeutics, Ed. 2, New York, The Macmillan Company, 1955, pp. 656-658.

36. Bernstein, C., and Klotz, S. D.: Use of Chlor-Trimeton in Allergic Diseases, with Special Reference to Its Injectable Administration, Ann. Allergy 10:479-483 (July-Aug.) 1952.

37. Jenkins, C. M.: A Small Dosage, Injectable Antihistamine (Chlor-Trimeton Maleate Injectable) in the Treatment of Allergic Diseases: Clinical Study, Ann. Allergy 11:96-103 (Jan.-Feb.) 1953.

38. Offenkrantz, F. M.; Margolin, S., and Jackson, D.: Prevention of Transfusion Reactions by Intravenous Chlor-Trimeton Maleate, J. M. Soc. New Jersey 50:253-255 (June) 1953.

Superior Vena Caval Replacement

I. Unsuitability of Free Tubes of Autogenous Pericardium

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While the clinical syndrome produced by obstruction of the superior vena cava may be quite disabling, it fortunately occurs with relative infrequency. Chronic mediastinal inflammation, malignant neoplasms, and aortic aneurysms appear to be the commonest causes of the obstruction. Although palliative efforts may be indicated in some cases of obstruction due to malignant tumor, the major therapeutic challenge concerns those cases in which the obstruction is due to benign, constrictive inflammatory changes in the mediastinum.

The reported clinical experience with superior vena caval replacement or by-pass has been somewhat discouraging. Deterling and Bhonslay,[2] in 1955, reviewed their experimental studies and the published clinical experience with superior vena caval replacement and concluded that partial or complete failure of the graft was the most frequent result.

It would appear, however, that autogenous tissue, especially autogenous venous tissue, should prove to be the most suitable material for superior vena caval grafting. It, furthermore, is desirable that the autogenous material should be available in the near proximity of the site of operation and that it be of sufficient size to form or to permit the construction of an adequate vascular conduit. Unfortunately, the intrathoracic blood vessels which might be used are either too small to serve for caval replacement or cannot be readily sacrificed. The pericardium remains as the major intrathoracic autogenous tissue which is of adequate size and may be sacrificed easily and safely for use in the construction of free tubes for caval vascular replacement. While tubes of pericardium have been used experimentally as aortic grafts, we have been unable to discover any reports of their use in venous replacement. The present study, accordingly, was carried out to evaluate the suitability of free tubes constructed from pericardium for superior vena caval replacement.

From the Department of Surgery, Indiana University Medical Center. Aided in part by grants from the National Heart Institute, National Institutes of Health, U. S. Public Health Service, and the Indiana Heart Foundation.

Material and Methods

Healthy mongrel dogs were used. The weight of the dogs ranged from 7 to 13 kg. A mixture of oxygen and ether, delivered through an endotracheal tube by means of a mechanical respirator, was employed for anesthesia following induction with intravenous thiopental (Pentothal). Although a right fourth interspace thoracotomy was used initially, it was soon realized that a third interspace incision provided much better exposure and greatly facilitated the completion of the more difficult superior anastomosis. Accordingly, the third interspace incision became the standard operative approach.

The pericardium was opened, and a large rectangular segment of pericardium was excised. The segment of pericardium was cleared of all fat and loose areolar tissue and was fashioned into a cylinder of desired size by wrapping it around a syringe barrel. The endothelial surface of the pericardium formed the inner lining of the cylinder. Barrels of both 2 and 5 cc. syringes were employed. Redundant pericardium was cut away, and the edges of the pericardial cylinder were approximated by means of a continuous everting mattress suture of 00000 arterial silk (Fig. 1). The superior vena cava was then dissected free from its surrounding tissue from the bifurcation of the innominate veins to the entrance of the vena cava into the right atrium. It was occluded just above the azygos vein and at the level of its bifurcation. Straight Potts multitoothed coarctation clamps, the blades of which were ensheathed

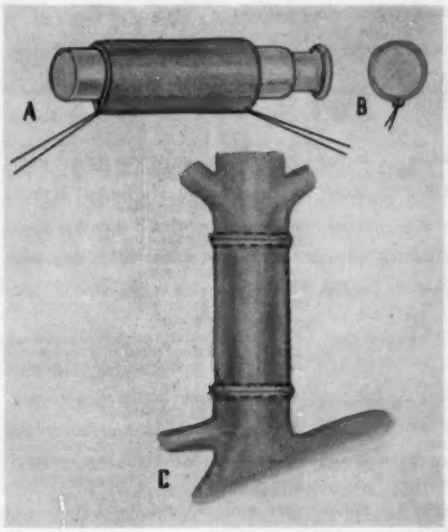

Fig. 1.—Drawings demonstrating technique of construction of free tube of pericardium and method of its use to replace resected segment of superior vena cava.

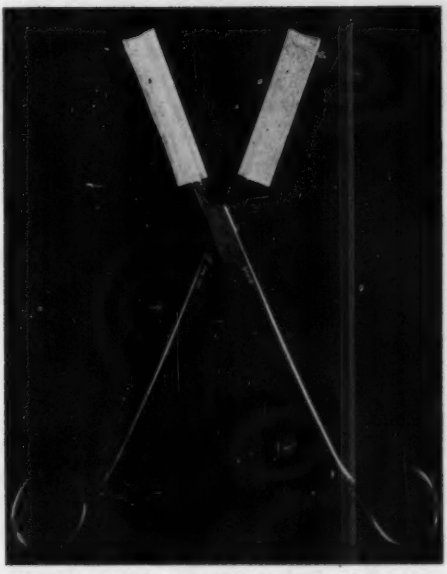

Fig. 2.—Photograph of Potts coarctation clamp showing sheaths of filter nylon fabric as used to cover blades.

in cylinders of nylon filter fabric, were employed for caval occlusion (Fig. 2). The ensheathing cylinder of filter fabric was of considerable aid in solving the problem of vena caval slippage through the occluding clamps.

The superior vena cava was resected from just above the azygos vein to just below its bifurcation and was replaced with the pericardial cylinder. The anastomoses were performed with a continuous everting mattress suture of 00000 arterial silk. During the placement of the graft, its inner surfaces were intermittently irrigated with an isotonic salt solution containing heparin. The period of vena caval occlusion required to complete the anastomoses varied from 28 to 52 minutes. Bleeding at the suture lines was seldom a problem. When it did occur, one or two additional sutures were adequate. The azygos vein was not ligated.

Immediate flow of venous blood through all of the grafts was excellent following release of the occluding clamps. Some graft pulsation was observed with right atrial contraction. Because of its thin wall and translucency, the appearance of the pericardial graft was strikingly similar to that of the replaced segment of vena cava. In one-half of the 12 animals operated upon, the pericardial cylinder was of the same diameter as that of the replaced vena cava. In one animal the graft was smaller than the vena cava, and in five it varied from slightly to significantly larger. In all of the animals the graft was patent and appeared to be functioning normally at the time of thoracotomy closure. The chest wall was closed in layers, and a catheter which was left in the chest during the closure was aspirated and withdrawn.

Results

All 12 animals survived the operation. Cavograms were carried out in 11 of them from three hours to three months following operation (Table). All 11 cavograms showed the grafts to be occluded. In some cavograms only the site of occlusion was shown (Fig. 3). In others the development of numerous collateral channels could also be demonstrated. Two animals died, 15 and 20 days after operation. The other 10 animals were killed, from six days to three months following operation. At postmortem examination, the graft was found to be completely occluded by thrombus formation in all 12 animals. In the majority of the dogs a significant amount of clear fluid was found in the chest. The veins of the neck were engorged, and in some of the animals there was a definite bulging of the eyes.

In only one animal, Dog 6, was the chest found to be free of fluid. This animal was

Summary of Results of Superior Vena Caval Replacement with Free Tubes of Autogenous Pericardium

Dog No.	Duration of Caval Occlusion, Min.	Immediate Flow Through Graft	Relation Size of Graft to Replaced Vena Cava	Interval, Operation to Cavogram	Cavogram Appearance of Graft	Animal Died or Killed	Interval, Operation to Death	Autopsy Findings
1	38	Excellent	Slightly larger	10 days	Occluded	Killed	15 days	Moderate amount of clear fluid in chest graft completely thrombosed
2	38	Excellent	Larger	23 days	Occluded	Killed	23 days	Moderate amount of clear fluid in chest; graft completely thrombosed
3	39	Excellent	Larger	15 days	Occluded	Killed	15 days	Moderate amount of clear fluid in chest; graft completely thrombosed
4	28	Excellent	Slightly smaller	24 days	Occluded	Killed	24 days	Large amount of clear fluid in chest; graft completely thrombosed
5	37	Excellent	Same size	16 days	Occluded	Died	20 days	Moderate amount of clear fluid in chest; graft thrombosed, with constriction at superior anastomosis
6	48	Excellent	Same size	3 mo.	Occluded	Killed	3 mo.	No fluid in the chest; marked enlargement of azygos; increased number of venous collaterals; graft thrombosed and constricted throughout
7	34	Excellent	Same size	10 days	Occluded	Died	15 days	Moderate amount of clear fluid in chest; graft completely thrombosed
8	55	Excellent	Slightly larger	21 days	Occluded	Killed	21 days	Moderate amount of clear fluid in the chest; graft completely thrombosed
9	56	Excellent	Same size	25 days	Occluded	Killed	44 days	Moderate amount of clear fluid in chest; graft thrombosed, with some constriction at both anastomatic ends
10	52	Excellent	Slightly larger			Killed	25 days	Graft completely thrombosed
11	48	Excellent	Same size	16 days	Occluded	Killed	15 days	Moderate amount of clear fluid in chest; graft completely thrombosed
12	38	Excellent	Same size	3 hr.	Occluded	Killed	6 days	Graft completely thrombosed

killed three months postoperatively. The azygos vein of this animal was approximately two times the normal size, and numerous collateral venous channels had formed. The thrombosed graft in this animal had become markedly constricted throughout and gave the appearance of a fibrous band.

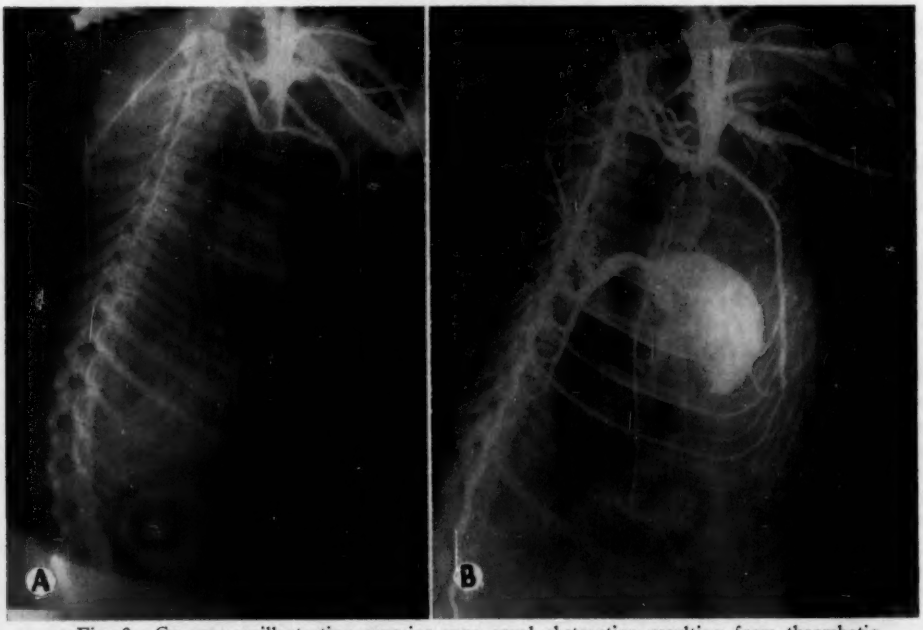

Fig. 3.—Cavograms illustrating superior vena caval obstruction resulting from thrombotic occlusion of pericardial tube grafts. Varying degrees of demonstrable collateral circulation are shown in *A* and *B*.

Comment

Although the tubes of pericardium immediately after placement bore a striking resemblance both in appearance and on palpation to the replaced segment of superior vena cava, the end-result was uniformly unsatisfactory, due to thrombotic occlusion of the graft in all of the animals. In one animal a cavogram showed occlusion of the graft as early as three hours after operation. The relation of the size of the graft to that of the replaced vena cava did not appear to affect the outcome.

We have been unable to discover any other reported experience with the use of autogenous pericardium in venous replacement. However, it has been employed both alone and supported by fascia or a nylon net in aortic replacement. Sako and Varco,[5] in 1953, found that pericardial tubes functioned satisfactorily when used as aortic grafts. Although there was some initial dilatation of the graft, it was felt that this initial dilatation was possibly due in part to inexpert matching of the two lumina. No further indication of progressive aneurysm formation was noted with the passage of time. They also found that a layer of supporting fascia lata prevented this initial dilatation. They questioned the need for a fascia lata buttress in the more precisely tailored grafts because of the apparent intrinsic resistance of pericardial segments to aneurysm formation. Adler,[1] in 1955, reported that pericardium supported by a nylon net served satisfactorily in aortic replacement. He called attention to the relative frequency of mural thrombi and lipid deposition on the walls of these pericardial grafts.

Free segments of pericardium have been used in this laboratory in several studies. The marked degeneration of tubes of autogenous pericardium employed as transventricular slings was similar to that encountered with transventricular slings of autogenous artery and of autogenous tendon.[4] Although free pericardium was successfully employed in the repair of experimentally created atrial septal defects in dogs,[7] its use in the attempted repair of atrial septal defects in human cases was disappointing.[6] Sacs made of free segments of pericardium and open at one end were used in dogs in attempts experimentally to create saccular aneurysms of the thoracic aorta. These attempts were consistently unsatisfactory, owing to relatively prompt thrombotic obliteration of the sac lumen.[3]

Summary

Endothelial-lined tubes made from free segments of pericardium were employed in experimental superior vena caval replacement in 12 dogs. There was no operative mortality. Although the immediate results appeared to be excellent with respect both to appearance and function, thrombus formation led to total occlusion of the grafts in all 12 animals. The occurrence of graft occlusion was established both by cavograms and by autopsy. These findings strongly suggest the unsuitability of free tubes of autogenous pericardium in superior vena caval replacement.

The use of sheaths of filter nylon fabric over the blades of the multitoothed Potts coarctation clamps is described. These sheaths greatly facilitated the gentle handling, without slippage, of the cut ends of the vena cava during resection and anastomosis.

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REFERENCES

1. Adler, R. H.: Autogenous Thoracic Aorta Grafts of Pericardium and Nylon Net Using a Thrombin-Fibrinogen Coagulum, J. Thoracic Surg. 30:513, 1955.

2. Deterling, R. A., Jr., and Bhonslay, S. B.: Use of Vessel Grafts and Plastic Prostheses for Relief of Superior Vena Caval Obstruction, Surgery 38:1008, 1955.

3. Moore, T. C.: Unpublished data.

4. Moore, T. C., and Shumacker, H. B., Jr.: Unsuitability of Transventricular Autogenous

Slings for Diminishing Valvular Insufficiency, Surgery 33:173, 1953.

5. Sako, Y., and Varco, R. L.: Long-Term Observations of Autogenous Pericardial and Venous Grafts in the Thoracic Aorta, S. Forum (1952), p. 136, 1953.

6. Shumacker, H. B., Jr.: Surgical Repair of Atrial Septal Defects, Ann. Surg. 138:404, 1953.

7. Shumacker, H. B., Jr.; Moore, T. C., and King, H.: Experimental Closure of Atrial Septal Defects, J. Thoracic Surg. 26:551, 1953.

A Histologic Study of the Tissues Surrounding Experimental Nylon Aortic Substitutes

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With the Technical Assistance of Carolyn Anderson, M.T., A.S.C.P.

Synthetic aortic substitutes have given relatively satisfactory early results and consequently are being used with increasing frequency. Many factors concerning the ultimate fate of these materials are yet to be determined. There is evidence that the fabric itself loses strength following implantation in aortas of experimental animals.[5] That aortic homografts fail to maintain their normal histologic configuration is now well established. Among the degenerative changes which have been observed are calcification, ulceration, loss of elastic tissue elements, and marked thinning of the wall.[2,4]

Observations over a two-year period of 17 dogs with nylon aortic substitutes were the subject of a previous report.[1] A presentation of the histologic characteristics of this material follows.

Materials and Methods

Animals were killed at intervals from 1 to 760 days after implantation of the nylon tubes into the abdominal aorta. The "grafted" segment along with 2 to 4 cm. of adjacent aorta at each end was removed and placed in 10% formalin solution. Representative samples of tissue were taken from the junction at each end and from the midportion of each "graft." They were embedded in celloidin, and sections 15μ in thickness were cut. Serial sections were prepared with hematoxylin and eosin, Gomori's trichrome stain, Verhoeff's elastic tissue stain with a Van Gieson counterstain, periodic acid-Schiff stain, and Wilder's silver impregnation method for reticular fibers. Seven representative specimens, including one thrombosed "graft," were studied.

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Results

Repair Around "Graft" Material.—In all specimens the nylon "graft" was enveloped in a sheath of connective tissue, the outer layer being thicker than the inner layer. From one area to another in each graft there was only slight variation in the thickness of both inner and outer layers. There was no consistent difference in the amount or nature of the material composing the sheath that could be related to the age of the nylon prosthesis. This connective tissue did not grow into the graft material to any extent, but was attached to its edges at regular intervals so as to present a scalloped appearance (Figs. 1 and 2). In this connective tissue there was a heavy formation of reticular fibers both inside and outside the graft material (Fig. 2). When the reticular fibers were compared with the over-all connective tissue as brought out by the trichrome stain, it was apparent that these fibers were the major component of the total connective tissue structure. No elastic connective tissue fibers could be demonstrated in either the outer or the inner sheath, this component of the adjoining aorta ending abruptly at the synthetic material (Fig. 1). Small blood vessels could be demonstrated in the tissue composing the outer sheath and were more prominent in the external portion of this layer. No blood vessels were seen in the connective tissue of the lumen side of the "graft."

Endothelial growth on the lumen side of the inner sheath was present in all grafts which were functioning at the time the animal was killed (Fig. 3). No endothelial elements were demonstrable in the animal

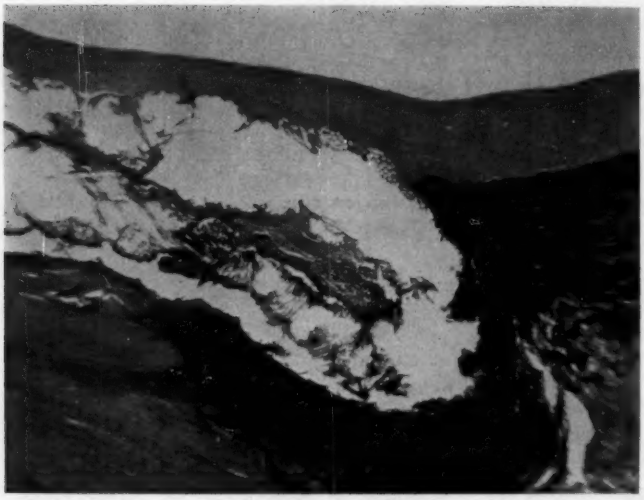

Fig. 1. — The elastic fibers of the host aorta end sharply at the prosthesis. Much of the nylon has been lost in the section, leaving the edges with a slight ingrowth of connective tissue at regular intervals, presenting a scalloped appearance. The small amount of connective tissue in the center is between the two layers of cloth, where a cuff was turned back to facilitate sewing. Elastic tissue stain; × 40.

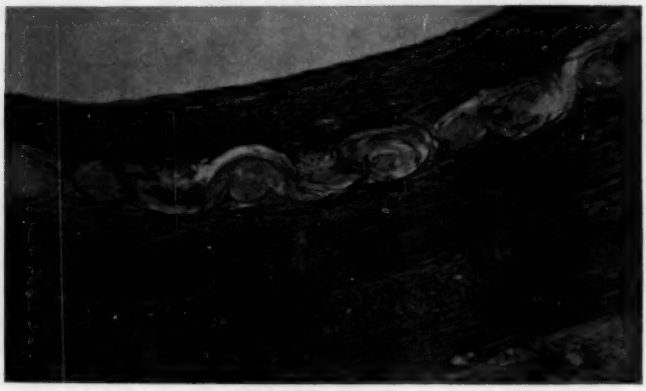

Fig. 2.—A dense collection of reticular fibers is present on both sides of the nylon "graft." Reticular fiber stain; × 40.

in which thrombosis had occurred (Fig. 4). The endothelial cells were quite flat throughout most of the sections but were more prominent and oval at some points, as in Figure 3.

Inflammatory and Degenerative Changes. There was slight focal infiltration of lymphocytes in the tissues around all of the "grafts" at scattered points. Moreover, there were areas of severe focal inflammatory reaction (Fig. 5) in the tissues surrounding all "grafts" except one (Dog 8). This process varied considerably in degree from one specimen to another and did not correlate significantly with the age of the graft. At some points the inflammatory process was present to a slight degree in a small area just beneath or along the endothelial layer, with this membrane remaining intact; this was in contrast to the more advanced lesions, where the endothelium was always absent. In the places where the endothelium was intact over or adjacent to the foci of inflammation, the cells of this structure were more apt to be swollen and more prominent. The inflammatory reaction extended in some areas to the outer fibrous sheath. This exudate was composed of a mixture of inflammatory cells, most of which were polymorphonuclear leukocytes. Occasional giant cells of the foreign body type, as well as immature fibroblasts,

Fig. 3.—A prominent endothelial membrane is present on the lumen side of the inner connective tissue sheath. Hematoxylin and eosin; reduced to 94% of mag. × 85.

Fig. 4.—An organizing thrombus is attached to the connective tissue inner sheath of the "graft" and the intima of the adjacent aorta. Hematoxylin and eosin; reduced to 94% of mag. × 40.

were also seen. No eosinophils were noted. In a few instances old hemorrhage, evidenced by a dark-brown pigment and macrophages, as well as small amounts of more recent hemorrhage, could be seen around the areas of inflammation (Table).

A striking feature of this inflammatory process was the presence of fibrinoid necrosis, which displayed a remarkable affinity for eosin in the hematoxylin-eosin preparations (Fig. 5). The inflammatory reaction and its accompanying necrosis completely

Fig. 5.—The endothelium and inner connective tissue membrane are absent over an area of fibrinoid necrosis in the inner part of the outer connective tissue sheath. The inflammation at this point is less severe than that seen in many other such areas. Hematoxylin and eosin; × 40.

Summary of Findings in the Tissue Surrounding Nylon Aortic Prostheses

Dog No.	Age of Grafts, Mo.	Endothelial Regeneration	Focal Endothelial "Ulceration"	Elastic Fibers	Hemorrhage	Fibrous Intimal Plaques (Aorta)
3	8	+	+	0	0	+
4	15	+	0	0	0	0
7	15	+	+	0	0	+
8	17	+	+	0	Slight (old)	+
5	18	+	+	0	Slight, periadventitial	+
2	24	+	+	0	0	+

Fig. 6.—X-ray of air-filled "graft."

Fig. 7.—A large intimal plaque overlies an incompletely destroyed internal elastic membrane in the aorta adjacent to one of the prostheses. This plaque was separated from the junction of aorta and "graft" by uninvolved intima. Hematoxylin and eosin; reduced to 94% of mag. × 85.

destroyed the connective tissue of the inner lining sheath, including the reticular fibers, in areas of severe involvement. Also, at these points it was noted that a portion of the reticular fibers of the inner surface of the outer sheath was also destroyed. No areas of calcification were seen, although a small focus of cartilaginous metaplasia was present on the lumen side near the anastomosis in one specimen (Fig. 6).

Intimal arteriosclerosis of the adjoining aorta, characterized by the presence of fibroelastic plaques of the intima, was present directly adjacent to, as well as away from, the junction of the host vessel and the nylon prosthesis. With the stains employed, these lesions were very similar to the early lesions of the intimal type of arteriosclerosis in man, but no obvious lipid content was present. Specific lipid stains were not utilized in the present investigation. The process was accompanied by a destruction of the internal elastic membrane only in the dog which had been followed for 24 months (Fig. 7). The elastic component of these lesions varied both within the same plaque and between different plaques.

Comment

When implanted in the aortas of normal dogs, nylon prostheses were rapidly incorporated by the tissues of the animal. The synthetic tube was completely lined within six months by a layer of tissue, the major part of which was composed of reticular fibers. This sheath was lined by endothelium. No blood vessels were seen in this layer of tissue, nor was it demonstrated that they grew through the nylon fabric.

Although comparatively minimal in most of the "grafts," there was inflammatory reaction around all specimens. Of particular interest were the degenerative areas of fibrinoid necrosis. These lesions were visible grossly, appearing as small, round areas of discontinuity of the inner lining sheath. The endothelium, as well as the reticulum of the fibrous tissue, had disappeared in these areas. The process also involved the inner portion of the outer sheath. The pathogenesis of these lesions is not known, but it would seem likely that the primary change was fibrinoid necrosis, the inflammation following. The inadequacy of the blood supply to these tissues offers a possible explanation of their development.

Whether or not these lesions would have ultimately caused rupture of the "graft" is not known. The importance of the synthetic material itself in maintaining the integrity of the new "vessel" in these areas is certainly emphasized. The resistance of the "graft" to arteriosclerosis, in contrast to the adjoining aorta, is again demonstrated.[3]

Unlike aortic homografts, calcification was not found to be a late degenerative change of synthetic prostheses.

Summary

Nylon aortic substitutes are enveloped by a fibrous sheath, which is laid down by the host. This new vascular conduit is lined by endothelium.

The sheath is composed for the most part of reticular fibers of connective tissue. No elastic fibers are found in the new vessels.

Occasional foci of fibrinoid necrosis and inflammation disrupting the continuity of the inner lining sheath are described.

Although arteriosclerotic plaques are present in the adjacent aorta, none are observed in the synthetic material.

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REFERENCES

1. Barnett, W. O.: Experimental Nylon Aortic Substitutes, A. M. A. Arch. Surg., to be published.

2. Coleman, C. C., Jr.; Deterling, R. A., Jr., and Parshley, M. S.: Some Long-Term Observations on Aortic Homografts, Surgery 37:64, 1955.

3. Creech, O., Jr.; Jordan, G. L., Jr., and DeBakey, M. E.: Effect of Chronic Hypercholesterolemia on Synthetic Aortic Substitutes, Surg. Gynec. & Obst. 104:385, 1957.

4. Hardin, C. A.: Orlon and Nylon Prostheses for Abdominal Aneurysms and a 5-Year Observation on Experimental Aortic Homografts, Ann. Surg. 146:78, 1957.

5. Harrison, J. H.: Use of Teflon as a Blood Vessel Replacement in Experimental Animals, Surg. Gynec. & Obst. 104:81, 1957.

Effect of Intravenous Nutrient Solutions on Ventricular Fibrillation in the Hypothermic Dog

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Introduction

A high incidence of ventricular fibrillation in dogs during general hypothermia at body temperatures below 28 C (82.4 F) has been reported.[1-4] A few pharmacological agents have been evaluated for their effects in reducing the incidence of fibrillation at low temperatures.[5,6] It is noteworthy that the agents so far reported were administered after the animal had reached the desired hypothermic level.

Recently, aminoacetic acid (glycine) was shown to be of thermogenic value by its ability to aid in rapid rewarming to normal body temperature.[7] Furthermore, a prolongation of cooling time was attributed to the aminoacetic acid administration, which began prior to ice-water immersion. Aminoacetic acid has also been shown to possess an antiarrhythmic effect in cyclopropane-epinephrine-induced ventricular arrhythmias[8] and in hypothermia.[9] Evidence, therefore, suggests that aminoacetic acid possesses both thermogenic and antiarrhythmic properties.

The present study was performed to test whether these effects were specific for aminoacetic acid or whether other nutrient materials, such as dextrose or fat, might have similar effects in hypothermia.

Method

Mongrel dogs, weighing 6.8 to 23.2 kg., were deeply anesthetized with pentobarbital sodium. An endotracheal tube was inserted, and the dog was artificially ventilated at 12-16 respirations per minute. Polyethylene catheters were inserted into the right femoral artery and vein. Following a control study, the dog was immersed in ice water, as previously described[1] and the nutrient administered intravenously.

Two control series of dogs were treated as follows: Eight dogs received saline in comparable volume to the dogs receiving nutrient, and six dogs were given similar amounts of nonmetabolizable polysaccharide (dextran). The three experimental groups received intravenously 1 gm. of nutrient per kilogram of body weight. The solutions used were 5% aminoacetic acid, 5% dextrose, and 15% fat emulsion (Lipomul, a 40% emulsion of vegetable oil in aqueous carbohydrate medium).

The rate of nutrient administration was determined by the rate of cooling. It was adjusted to terminate when the rectal temperature had reached 26 C (78.8 F). At this time the dog had received the calculated amount (1 gm/kg.).

The dog was removed from the bath at 26 C. After 10 to 15 minutes, the rectal temperature had dropped another 1-3 degrees (C), where it remained during the operation. The hypothermic range finally achieved, therefore, was between 23 and 25 C (73.4 and 77 F).

Using sterile surgical technique, a right anterolateral thoracotomy incision was made through the fifth intercostal space. After entering the thorax, the pericardial sac was opened widely. The superior and inferior venae cavae adjacent to the atrium were encircled with umbilical tapes and inflow occlusion established. A 5 cm. incision was made in the right ventricle, followed by digital exploration of the ventricular cavity. These manipulations have been shown to produce uniformly fibrillation in the unprotected cold dog.[5] Six to seven minutes later the ventricular wall was sutured and the pericardial sac loosely closed. After exactly 10 minutes of occlusion, inflow was reestablished by release of the tapes. The thorax was closed, and the dog was then immersed in warm water 42 to 45 C (107.6 to 115 F).

Observations were made on all dogs at normothermia, 30 and 26 C, surgical temperature, and 30 and 35 C. Pressures were transmitted to an un-

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Summary of Data *

Treatment	Dogs	Ventricular Fibrillation	Resuscitation	Alive Seven Days
Saline (control)	8	8	0 of 6 attempts †	0
Dextran (control)	6	5	0 of 4 attempts	0
5% dextrose	12	5	3 of 3 attempts	10
5% aminoacetic acid	11	4	2 of 2 attempts	9
15% fat	8	4	2 of 2 attempts	0 ‡

* Right ventriculotomy was used as fibrillatory stimulus in dogs at a temperature of 23-25 C following various solutions administered during cooling.
† On some occasions a defibrillator was not available.
‡ All animals died of pulmonary fat emboli.

bonded strain gauge and amplified and recorded on a multichannel oscilloscope-type recorder. Lead II of the electrocardiogram was monitored continuously on an oscilloscope. Records were taken of cooling times on all dogs.

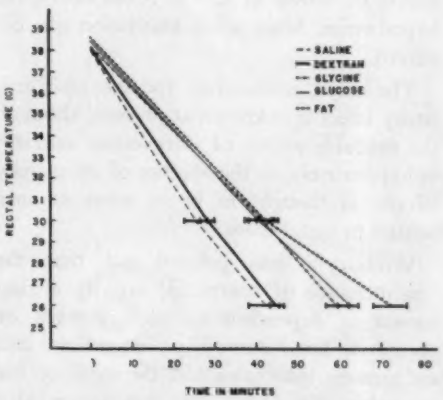
In all experiments, as is standard policy in our laboratory, an animal must live at least seven days to be considered a survival. An animal may live one, three, or five days postoperatively, yet die of a condition referable to the original surgical procedure.

Results

Data were obtained on 45 animals. The experiments were done in October, November, and December, 1956, in Denver. The accompanying Table summarizes the cardiac action following right ventriculotomy. There is little doubt that right ventriculotomy in the dog at temperatures below 26 C is a potent fibrillatory stimulus. Furthermore, resuscitative measures are of little avail in this temperature range in our laboratory. Eight of the eight saline-treated dogs showed ventricular fibrillation, and cardiac resuscitation proved uniformly unsuccessful. Five of the six dogs treated with dextran displayed ventricular fibrillation, and cardiac resuscitation was ineffective.

The dogs treated with nutrients were less vulnerable to the cardiac fibrillatory stimulus. Five of the twelve dextrose-receiving dogs showed ventricular fibrillation, an incidence of 42%. Three of three attempts to resuscitate the heart, using massage plus electric shock, proved successful. The aminoacetic acid group, consisting of 11 dogs, responded similarly to the surgical stimulus. Four of the eleven went into ventricular fibrillation (36%), and two of two attempts at cardiac resuscitation were successful. Of the fat-receiving dogs, 50% showed ventricular fibrillation, and two of two attempts to resuscitate the heart proved successful. It is to be noted, however, that there are no seven-day survivals in the fat-receiving group. Unlike the other two experimental series, survival time was limited to a few hours after surgery, six of the dogs dying within four hours. Autopsy revealed massive fat embolization in the lungs. Apparently, hypothermia changed the suspension characteristics of this emulsion, releasing free fat globules, since this per cent solution, in the amount and rate of administration used, is readily tolerated by the warm animal.

The Figure represents the mean cooling times for the nutrient and control groups. The individual nutrients significantly prolonged the cooling time. The average time required to cool eight control dogs to 26 C was 45 minutes. The fat-, aminoacetic acid-, and dextrose-receiving dogs required 72, 59, and 62 minutes, respectively, to cool to



Graphic presentation of the effect of nutrient materials upon the cooling time of the dog.

a rectal temperature of 26 C. An increase of 27 minutes is evidence for fat ($P<0.01$), of 13 minutes for aminoacetic acid ($P<0.01$), and of 17 minutes for dextrose ($P<0.01$).

The cooling rates of dogs receiving aminoacetic acid, fat, and dextrose were similar until a rectal temperature of 30 C was reached. For aminoacetic acid the rate was 0.19 degree (C) per minute; dextrose, 0.21 degree per minute; fat, 0.20 degree per minute. The controls cooled at the rate of 0.30 degree (C) per minute. From a rectal temperature of 30 to 26 C aminoacetic acid, dextrose, and fat required 0.23, 0.19, and 0.13 degree (C) per minute, respectively. The controls cooled from 30 to 26 C, at the rate of 0.22 degree (C) per minute.

Blood pressure and heart rates were taken, but the data are not presented. In these experiments, nutrient administration had no effect on blood pressure or heart rate. On the basis of these indices, it appeared, therefore, that no significant circulatory change was effected by this administration.

Comment

Dextrose, aminoacetic acid and fat, when administered intravenously, all demonstrate a prophylactic antifibrillatory effect in the hypothermic dog undergoing right ventriculotomy. Dextrose has also been found useful by Mavor et al.[10] in resuscitating the hypothermic heart after fibrillation has occurred.

The exact mechanism for the antifibrillatory effect is unknown at present, although the probable action of intravenous nutrient in hypothermia, in the absence of circulatory effects, is thought to be in some manner related to metabolism.

Winbury[11] has pointed out that the "maintenance of contractile activity during anoxia is dependent on the reserves of phosphate bond energy, on exogenous and endogenous substrates and the capacity for anaerobic glycolysis." He has shown also that the rate of anaerobic glycolysis in mammalian cardiac muscle is inadequate to support contractile activity. However, with exogenous glucose present during the anaerobic period, he noted that the rate of glycolysis is sufficient to maintain the functional integrity of the contractile mechanism.

In view of the above, one might speculate that the hypothermic dog receiving intravenous nutrient may well build up glycogen stores in the myocardial tissue which he later uses during the anoxic period of circulatory occlusion. Furthermore, under these conditions, the rate of anaerobic glycolysis during the period of circulatory occlusion may well be sufficient to maintain contractile activity in the hypothermic animal.

The more prolonged cooling time due to the specific dynamic action of aminoacetic acid, as reported by Beavers et al.,[7] is not evident in our experiments. Any nutrient in higher-than-normal concentrations in the blood will apparently alter cooling rates.

On the basis of these studies, we feel at the present time that intravenous nutrient administration should be a standard adjunct to the induction of hypothermia, that it should be continued until circulatory occlusion is instituted and should be resumed after the release of occlusion. This has long been our clinical custom on a hitherto empiric basis.

Summary

Five groups of dogs undergoing hypothermia and a standardized cardiac operation at 23-25 C were studied. The groups differed only in the type of intravenous fluid being administered during the cooling period of ice-water immersion. The fluids were 0.9% sodium chloride, 5% dextran, 5% aminoacetic acid (glycine), 5% dextrose, and 15% fat emulsion (Lipomul).

The dogs receiving nutrient fluids all showed a significant increase in cooling time. A marked decrease in the incidence of ventricular fibrillation was observed, and, when fibrillation occurred, resuscitation was uniformly successful.

The mechanisms responsible for these effects are under investigation.

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REFERENCES

1. Swan, H.; Zeavin, I.; Holmes, J. H., and Montgomery, V.: Cessation of Circulation in General Hypothermia: Physiologic Changes and Their Control, Ann. Surg. 138:360-376, 1953.

2. Cookson, B. A.; Neptune, W. B., and Bailey, C. P.: Hypothermia as Means of Performing Intracardiac Surgery Under Direct Vision, Dis. Chest 22:245-260, 1952.

3. Bigelow, W. G.; Mustard, W. T., and Evans, J. G.: Some Physiologic Concepts of Hypothermia and Their Applications to Cardiac Surgery, J. Thoracic Surg. 28:463-480, 1954.

4. Edwards, W. S.; Simmons, E.; Lombardo, C. R.; Bennett, A., and Bing, R. J.: Coronary Flow in Hypothermia: Incidence of Ventricular Fibrillation with Decreased and Increased Flow, A. M. A. Arch. Surg. 71:853-862, 1955.

5. Montgomery, A. V.; Prevedel, A. E., and Swan, H.: Prostigmine Inhibition of Ventricular Fibrillation in the Hypothermic Dog, Circulation 10:721-727, 1954.

6. Baer, S. B.; Montgomery, A. V.; Blair, E., and Swan, H.: Relation of Coronary Blood Flow to Prevention of Ventricular Fibrillation in the Cold Canine Heart, S. Forum (1955) 6:200-203, 1956.

7. Beavers, W. R., and Covino, B. G.: Immersion Hypothermia: Effect of Glycine, Proc. Soc. Exper. Biol. & Med. 92:319-322, 1956.

8. White, C. W., and Stutzman, J. W.: The Protective Effects of Glycine, Glycolic and Acetic Acids and Their Salts Against Cyclopropane-Epinephrine Ventricular Arrhythmias, Arch. internat. pharmacodyn. 82:416-424, 1950.

9. Beavers, W. R., and Covino, B. G.: Antifibrillatory Effects of Glycine in Hypothermia, Fed. Proc. 16:281, 1957.

10. Mavor, G. E.; McEvoy, R. K., and Mahoney, E. B.: Effectiveness of Hypertonic Glucose in Resuscitation of the Hypothermic Heart Following Potassium Chloride Arrest, Circulation Res. 4:389-393, 1956.

11. Winbury, M. M.: Influence of Glucose on Contractile Activity of Papillary Muscle During and After Anoxia, Am. J. Physiol. 187:135-138, 1956.

Primary Resection of Descending Colon for Obstructing Annular Carcinoma

Occurrence in a Seventeen-Year-Old Youth

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Carcinoma of the colon without preexisting polyposis or chronic ulcerative colitis is unusual under the age of 40, rare under the age of 30, and almost nonexistent under the age of 20. The present case report is submitted because of the rarity of the condition in a teen-age patient, and because of the controversial method of surgical treatment, namely, the primary radical resection of the unprepared obstructed colon, without complementary colostomy.

None of the references consulted specifically mentioned such a malignancy in the age decade of the patient. Shallow et al.,[7] in their review of 750 cases of colon carcinoma, mention the low age extreme as 16 years. However, their cases of polyposis were not distinguished. Michel's[4] youngest patient with carcinoma (not otherwise specified) in 103 reported cases of acute colon obstruction was 13 years old. Sadler and McSwain[5] mention their youngest patient among 251 cases of colonic, rectal, and anal cancer as being 20 years old. The youngest in the series of 486 cases reported by Vynalek et al.[8] (in a 15-year review of colon carcinoma) was 21 years of age.

Colon surgery is now 60 years old.[1] The method of treatment of the present case represents perhaps the latest definitive step in the evolution of colonic surgery. Chase and Ferguson's[2] revolutionary paper on the primary resection of the obstructed colon places emphasis on adequate operative decompression and the liberal use of antibiotics at and after surgery. Their notable record concerns the primary resection of 7 obstructed right colons, with no deaths, and 10 obstructed left colons, with one death. The statistics of Michel and McCafferty[3] are pertinent. They point out that 90% of the postoperative deaths occur in the age group over 50, with two-thirds of the deaths over the age of 70.

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Report of Case

A 17-year-old Negro youth was admitted to Hermann Hospital on Oct. 11, 1956, with the complaint of cramping abdominal pain, distention, and blood in the stool.

He had been entirely well until Oct. 5, 1956, when a cramping epigastric pain occurred. This recurred and necessitated his doubling up or lying on his side for relief. He had no nausea, but vomited green, bitter material on two occasions. His last bowel movement was brown and formed and was passed on Oct. 4. From Oct. 6 through Oct. 8 he was not particularly ill, but had occasional cramping pain and ate only crackers and fluids. A soapsuds enema was returned mixed with bright red blood and mucus. On Oct. 9, the severity of the pains increased, and distention of the abdomen was noted. On Oct. 10, pain and distention had increased to a point where he was refusing anything but small amounts of broth.

The family history is noncontributory. The patient is the sixth of nine living, healthy children of healthy parents.

Examination of the patient at 5 p. m. on Oct. 11 revealed a husky, well-developed, well-muscled Negro youth whose nutrition and hydration belied his recent history of limited intake. The temperature was 98.4 F, pulse 110, respiration 12, and blood

OCTOBER	11	12	13	14	15	16	17	18	19	20
Urine sg	1026		1028							
Ur WBC	0		4-6							
Ur RBC	0		2-3							
Ur alb	0		1							
Hb	12.6	140	149	108	11.8				102	
Hemat		50	49	37	37.5				33	
RCB	3.8	5.1	5.0	3.8					3.6	
WBC	9.3	326		323					155	
Stabs	11	35		0					0	
Segs	52	54		94					78	
Lymphs	26	4		2					13	
Monos	11	6		3					3	
Eos	0	0		1					4	
Basos	0	0		0					2	
Tot Eos		0		233	144	144		344	400	377
BLOOD (mEq./L.)										
Chloride	93	82	112		103	92				
CO 2 vol %	64	41	50			47				
Sodium		130	117		127	132				
Potassium		4.2	4.1		4.4	5.2				
URINE (mEq./L.)										
Ur Na			38	56	140					
Ur K			78	46	40					
Ur Cl			68	137	188					
Solu-Cor	100	100	0	25	0	0	0	0	0	0
Blood	1000									
Hi Pulse		160	120	114	108	100	102	104	104	130
Lo Pulse		100	96	92	88	78	96	72	80	78
Hi Temp		103°	100°	100.8	100.8	101.4	100.6	100.8	99.8	99°
Lo Temp		98.8	98.2	99°	98.8	97.8	98.6	98.2	98.2	98°
Diet		NPO	NPO	NPO	NPO	LIQ	SOFT	SOFT	SOFT	GEN
Rectal Lavage		NO	YES	YES	YES	NO	NO	NO	NO	NO

OPERATION

EKG on 10/12 showed sinus tachycardia and non-specific T wave changes

Fig. 1.—Chart of quantitative values during hospitalization.

pressure 136/74. He appeared healthy except for an expression of anxiety, a distended abdomen, and an obvious preference to lie quietly on his left side. The tongue was moist and the skin normal. Positive findings were confined to the abdomen. Moderate generalized distention was present. Generalized minor tenderness and rebound tenderness were noted. Loud gurgling, infrequent peristalsis was heard even without the use of a stethoscope. The pelvic peritoneum on rectal examination had a degree of tenderness consistent with the generalized tenderness.

Laboratory findings are recorded on Figure 1.

X-rays of the abdomen showed multiple loops of distended bowel with an abrupt cessation of the gas shadow in the left colon. The films were not diagnostic, but were suggestive of obstruction in the descending colon.

Preoperative preparation consisted of eight hours of gastric suction, 1500 cc. of isotonic saline, and the commencement of parenteral administration of penicillin, streptomycin, and chloramphenicol (Chloromycetin) in high doses.

A right paramedian muscle-retracting incision was made. When the true condition was recognized, the incision was extended once for adequate exploration, and again for adequate dissection. A typical annular (napkin-ring) growth was found obstructing the colon at the junction of the upper and the middle third of its descending portion. The colon distal to the lesion was normal and collapsed. The colon proximal to the lesion was moderately distended, with thick pliable walls and a healthy color. The severest distention was present in the small bowel, the ileocecal valve being incompetent.

Fig. 2.—Preoperative x-ray appearance in supine position, suggesting left colon obstruction. Note abrupt cessation of gas shadow in left side of abdomen.

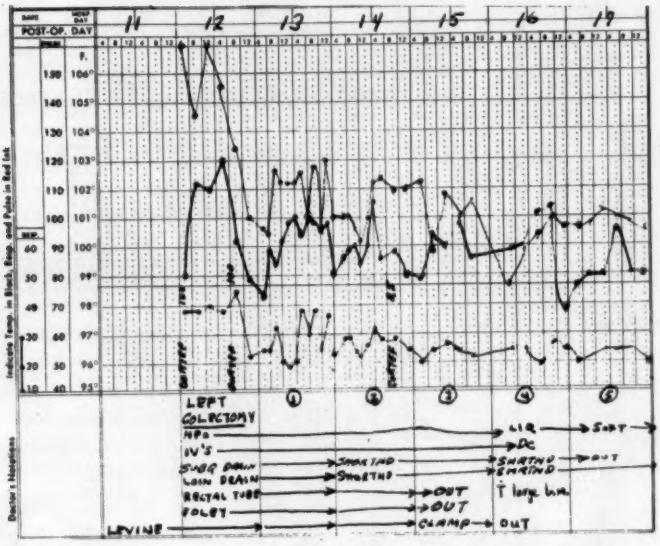

Fig. 3.—Graphic chart through fifth postoperative day.

Effective decompression of the small bowel was carried out by inserting the Barnes intestinal decompressor. Decompression of the large bowel was also accomplished by threading the instrument through the ileocecal valve and milking the colonic contents toward it.

At this point, the decision was made to perform a radical primary resection. The entire bowel was well decompressed; the exposure to the left abdomen was excellent, and the patient's condition under anesthesia left nothing to be desired. After mobilization of the lesion, a moment's hesitation confirmed the good condition of the patient; the possibility of carrying out the Mikulicz or Rankin operation was rejected, and the patient was committed to a primary radical resection. The colon was removed from the middle colic artery, to and including the area supplied by the first sigmoid artery. All mesentery and surrounding tissue were excised en bloc down to the inferior mesenteric artery. An open end-to-end anastomosis was done, using an external row of interrupted 0000 black silk sutures and an inner row of continuous 000 chromic absorbable surgical (gut) sutures. Reperitonealization was done. A flank drain to the dissected area was placed. Neomycin sulfate, 2.0 gm., was injected into the colon proximal to the anastomosis. At the end of the second hour of this four-hour operation, 100 mg. of hydrocortisone sodium succinate (Solu-Cortef) was given intravenously. Two pints of blood (1000 cc.) was administered during the procedure.

Postoperatively, a rectal tube was inserted, left in place, and gently lavaged by a house doctor about every two hours with a 1% solution of neomycin sulfate in isotonic saline. Wangensteen suction and antibiotics were continued. During the first few lavages, copious quantities of feces and gas were obtained; later, very little of either was produced. A Foley catheter was inserted to keep accurate records of urinary output.

Tachycardia, with a rate of 130 to 160 a minute, occurred during the first 12 hours. This rate fell to 90 to 120 a minute during the first five postoperative days. The temperature never exceeded 103 F, and this fell by lysis during the first five postoperative days. Intravenous hydrocortisone sodium succinate was given in the dose of 100 mg. 12 hours following surgery and of 25 mg. additionally on the second postoperative day. The Levin tube, Foley catheter, and rectal tube were discontinued on the third postoperative day. Oral feedings were started on the fourth postoperative day, and progressed to a general diet on the eighth day. A spontaneous bowel movement was passed on the fourth day, and daily thereafter. Antibiotics were discontinued on the eighth day. The patient was discharged on the 15th postoperative day, after showing no adverse signs or symptoms during the last week of hospitalization.

The pathological report described an adenocarcinoma of the colon with tumor in 3 of 22 lymph nodes examined. The gross specimen consisted of an annular, obstructing carcinoma, 4.5 cm. in length, with 15.5 cm. of normal bowel proximally and 8.0 cm. of normal bowel distally.

The patient, when last seen, on Sept. 1, 1957, had returned to full activity and was an apparently healthy and normal boy.

Fig. 4.—Obstructing annular adenocarcinoma of descending colon removed from 17-year-old Negro youth.

Comment

This patient was obviously in precarious straits the first one or two postoperative days. His clinical findings pointed to a battle with sepsis. Many authorities [2,6,9] condone this radical approach to the obstructed colon in carefully selected cases. A good preoperative condition, decompression at operation, and use of antibiotics seem to be the common denominator in successful treatment.

Summary

A case of obstructing adenocarcinoma of the descending colon in a 17-year-old Negro youth is presented. Neither polyposis nor ulcerative colitis was present.

A controversial method of surgical treatment was employed. The obstructed, unprepared colon was submitted to immediate resection with primary open anastomosis without complementary colostomy.

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REFERENCES

1. Burgess, A. H.: Discussion on the Treatment of Obstruction of the Colon, Brit. M. J. 2:547, 1923.

2. Chase, W. W., and Ferguson, W. H.: Emergency Colon Resection With Primary Open Anastomosis Without Preoperative Antibiotic Therapy, Am. Surgeon 21:928, 1955.

3. Michel, M. L., and McCafferty, E. L.: Acute Obstruction of the Colon, with Special Reference to Factors of Mortality, A. M. A. Arch. Surg. 57: 774, 1948.

4. Michel, M. L.; Thompson, C. T.; Reinstine, H. W., Jr.; Senter, R. R., and Dale, D. B.: Acute Obstructions of the Colon, Ann. Surg. 139:806, 1954.

5. Sadler, R. N., and McSwain, B.: Carcinomas of the Colon, Rectum and Anus, Am. Surgeon 21: 975, 1955.

6. Seybold, W. B.: Personal communication, 1956.

7. Shallow, T. A.; Wagner, F. B., Jr., and Colcher, R. E.: Clinical Evaluation of 750 Patients with Colon Cancer, Ann. Surg. 142:164, 1955.

8. Vynalek, W. J.; Saylor, L. L., and Schrek, R.: Carcinoma of the Colon: Statistical Analysis, Surg. Gynec. & Obst. 84:669, 1947.

9. Waldron, G. W.: Personal communication, 1956.

Intrathoracic Tension Phenomena in the Neonatal Period and Infancy

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A number of processes may result in pulmonary tension phenomena or tension pneumothorax in the neonatal period and in infancy. Localized hypertrophic emphysema, progressive infantile emphysema, obstructive lobar emphysema, and congenital pulmonary cysts are some of the diagnostic terms encompassing essentially indistinguishable clinical and roentgenographic entities. Hypoplasia of the lung with compensatory emphysema in adjoining pulmonary tissue may also be postulated in such instances. Congenital diaphragmatic hernia, with loops of gas-filled bowel protruding into the chest, may be confused clinically and on x-ray films with tension pulmonary cysts or bullous emphysema.

Although the primary lesions may vary, the assorted processes producing tension dynamics in the lung or pleural space of the infant result in clinical pictures sufficiently similar to warrant their collective consideration. Our experience with five consecutive patients, of ages 6 days to 4 months, in extremis from progressive tension states illustrates this surgical indication.

Report of Cases

CASE 1.—A 14-day-old, 7½ lb. (3402 gm.) boy was transferred from another hospital, where since birth he had had respiratory difficulty and cyanosis, requiring continuous oxygen. No forceful resuscitative measures were carried out at delivery. Roentgenograms taken on his first day of life showed multiple radiolucent areas in the left chest, felt to represent a diaphragmatic hernia. Celiotomy, carried out on his third day, revealed no diaphragmatic defect. He continued to do poorly, respiratory distress increasing despite two thoracenteses, which released air under considerable pressure. Upon transfer to the North Carolina Baptist Hospital, the infant was cyanotic and extremely dyspneic, apparently moribund. Films showed multiloculated rarefied areas in the left chest with marked displacement of the heart shadow toward the right (Fig. 1).

Thoracotomy was carried out six hours after admission. A large cystic lesion was found in the upper portion of the left lung, the remainder of which was completely atelectatic and devoid of fissures, lobes, or recognizable landmarks. There was complete absence also of the anterior mediastinal partition. The cystic area was resected, bronchiolar leaks being closed with suture ligatures. Respiratory function was remarkably im-

Figure 1

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proved immediately after operation. Alveolar air leaks, however, required prolonged thoracotomy tube suction and multiple thoracenteses, the child finally being discharged on his 32d postoperative day.

The resected specimen contained multiple cysts of typical bronchogenic structure lined with bronchial epithelium.

At age 6 months, bronchograms revealed the left bronchial anatomy to be markedly anomalous. He has grown and developed normally, has not had more than the usual childhood respiratory infections, but does have occasional nonproductive cough. He is now 5 years old.

CASE 2.—A 10-day-old boy, weight 6 lb. 5 oz. (2923 gm.), was admitted with a history of labored respiration and cyanosis, requiring oxygen therapy since birth. Gestation and delivery were normal. There was no knowledge of forced resuscitation. Roentgenograms made the first day of life showed a giant cyst in the right lung. He had been treated by thoracentesis and oxygen therapy until admission. Roentgenograms (Fig. 2) made the 10th day showed the heart shadow to be markedly shifted toward the left by tension cysts, occupying almost the entire right chest. Intracavitary tube suction was instituted in an attempt to decompress the right thorax. This failed to accomplish improvement, another cystic area ballooning up

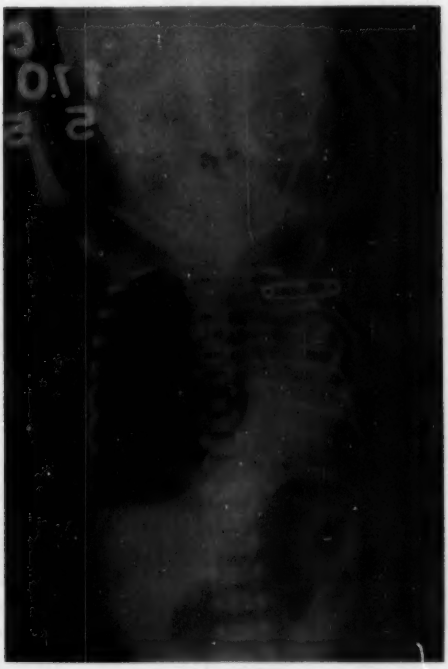

Figure 2

Figure 3

immediately after each insertion of the tube. Forty-eight hours after admission thoracotomy was carried out. The right middle lobe was found to be the site of multiple tension cysts, filling the hemithorax. The upper and lower lobes were thin and airless, resembling leaves. Right middle lobectomy was performed and the upper and lower lobes immediately expanded. His postoperative condition was excellent and his course uneventful.

The resected lobe was found to contain many cystic spaces microscopically characteristic of the bronchogenic type. He has grown and developed normally and is now 4½ years old.

CASE 3.—A 4-month-old girl was admitted with a five-day history of mild upper respiratory infection, coryza, slight cough, and wheezing and grunting respiration. Gestation and delivery had been uncomplicated and normal respiration spontaneous. There was obvious severe dyspnea, with marked diminution in breath sounds in the right chest. Roentgenograms (Fig. 3) revealed the heart to be shifted toward the left by an emphysematous middle lobe, which very nearly filled the right chest. She failed to improve after signs of infection had disappeared, and surgery was felt to be indicated.

A right posterolateral thoracotomy was carried out, and the right middle lobe was found to be extremely emphysematous, filling practically the entire right thorax. The upper and lower lobes were compressed and atelectatic. No definite

Figure 4

cystic lesions were apparent, nor was there bronchial compression; and it was felt that the emphysematous process in the right middle lobe might well be reversible. Accordingly, the middle lobe was compressed with the hand while the upper and lower lobes were allowed to expand. Satisfactory inflation was accomplished and the three lobes restored to their normal size and relationships within the pleural cavity. Expansion was maintained, and she was discharged on her 11th postoperative day. Approximately two and one-half years have passed since operation, and she continues to do well. Her chest film remains normal, and she has had no further pulmonary symptoms.

Case 4.—A 7½-week-old girl was admitted because of recurrent respiratory distress, cyanosis, convulsive seizures, and associated intermittent loss of consciousness since she was 2 weeks of age. There had been some difficulty in initiating satisfactory respiration at birth, but the methods employed were unknown. She was deeply cyanotic on admission, was struggling for breath, and ventilation was audible over the lower left chest only. X-ray films (Fig. 4) showed the right chest to be filled with tension cysts, which herniated across the mediastinum, displacing the heart and resulting in compression atelectasis of the left upper lobe. Continuous oxygen therapy and thoracentesis failed to accomplish improvement.

Thoracotomy was carried out 48 hours after admission. Immediately after the pleura was opened, the child's condition improved considerably. The right chest was almost completely occupied by a cystic-appearing, massively overinflated right lower lobe. The upper and middle lobes were completely atelectatic. Right lower lobectomy was easily accomplished and the upper and middle lobes expanded. Postoperative recovery was entirely uneventful. She has remained well for the year and a half since discharge.

Examination of the specimen disclosed a multiloculated cystic structure occupying principally the superior segment. The superior segmental bronchus was thought to be narrowed near its orifice, but no specific pathologic lesion was discernible. The cystic spaces were lined with alveolar epithelium.

Case No. 5.—A 3-day-old boy was admitted with the history of rapid, shallow respiration and intermittent cyanosis since the day of delivery. He weighed 7 lb. 5 oz. (3317 gm.), and delivery was normal, no forceful resuscitative measures being necessary. He was in extremely poor condition, cyanotic and limp, with 120 respirations per minute. Respiratory exchange was inaudible in the right chest and could only barely be heard in the left apex. Films (Fig. 5) showed the heart to be markedly displaced toward the left by multiple cysts occupying the entire right chest and extending across the midline. With continuous oxygen (Isolet) his color improved and respiration slowed somewhat.

After two days without further improvement or change in roentgenographic findings, operation was felt mandatory and was carried out on his sixth day of life. The right lower lobe was found to be

Figure 5

enormously distended, at the expense of totally airless middle and upper lobes. A loculated cystic process was apparently confined to the basal segments, which were removed. The superior segment and the medial basal segment appeared normal and were allowed to remain. The postoperative course was complicated by considerable difficulty with air leak, but he remained afebrile and did well despite a small residual space at the right base anteriorly. Approximately two weeks after discharge he was readmitted in marked respiratory distress with a massive right pneumothorax. Thoracotomy again was carried out, and a large cystic area was found in the remaining portion of the lower lobe. A small infected space was found between this structure and the diaphragm, communicating with the multilocular cyst. Right lower lobectomy was completed and the upper and middle lobes expanded. The postoperative course was essentially uneventful.

Specimens removed at both procedures contained congenital cysts lined with bronchial epithelium, with smooth muscle in the walls. Cystic disease, not visible or palpable at the first procedure, was missed in an effort to spare as much normal lung as possible. Bronchiolar leak from an incompletely excised cyst was thought to account for the small empyema space, and rupture of one of the cystic areas, for the sudden pneumothorax.

Comment

Various etiologic mechanisms have been indicted as responsible for tension cysts or emphysema in the infants and the newborn. Intrinsic ball-valve bronchial obstruction due to unusually flaccid bronchi,[11] the absence of cartilagenous rings,[6] or mucosal folds [9] have been described. Ehrenhaft and Taber [8] have demonstrated a correlation with forceful resuscitative methods employed at delivery. The occurrence of congenital pulmonary cysts, with bronchial-wall structure and bronchial epithelium, is well documented [2,5,7,8,10] and also may produce this syndrome. Extrinsic bronchial obstruction, caused by pressure of a vascular structure, such as a patent ductus arteriosus [4] or an enlarged pulmonary vein,[9] has also been reported as a cause of obstructive emphysema. Cystic spaces may develop in the lungs of children as sequelae of pneumonitis and bronchiolitis, and the spontaneous disappearance of these lesions has been reported.[1] This is a problem quite different from the progressive tension phenomena, which demand more aggressive treatment. In any form of check-valve bronchial obstruction, tension pneumothorax is an additional hazard to be considered.

These babies exhibited marked respiratory difficulty, and in four of the five instances the ventilatory impairment was an immediate threat to life. There were marked dyspnea, shallow respiration, cyanosis, and near-exhaustion. Auscultation revealed a remarkable diminution of breath sounds, exchange occasionally being practically inaudible. The large air-filled cysts or massive emphysematous distention of the lung, with areas of compression atelectasis, are quite impressive on the roentgenograms. Marked mediastinal shift may occur, due to herniation of involved lung into the opposite chest or to tension pneumothorax.

The rapid deterioration or obvious intractability of the process, despite conservative management, argued against persistence in only limited supportive measures. Although spontaneous closure of pulmonary cysts has been described, the progression of tension dynamics obviously necessitates intervention.

Thoracentesis may accomplish immediate life-saving decompression of cysts and pneumothoraces, but in this experience failed to achieve more than transient improvement. Pneumothorax and persistent air leak from puncture of cyst walls by the aspirating needle were quite troublesome and dangerous. Intracavitary suction was disappointing in that collapse of one cystic space simply permitted expansion of another of the multiloculated structures. Control of the immediate problem by either of these methods does nothing to correct the cause and hence is no guarantee against reinflation of the tension lesion or the sudden occurrence of catastrophic pneumothorax. Obstructive emphysema obviously requires definitive treatment. Bronchoscopy is a hazardous and unwarranted procedure in these seriously ill infants.

Thoracotomy was accordingly felt to be an urgent necessity. In some instances increased respiratory difficulty followed intubation of the trachea, and this was ascribed to further inflation of cystic or emphysematous lung at the expense of the remaining normal parenchyma. As soon as the thorax was opened and the compromised lung expanded, improvement was immediate.

In four instances the process was found to be limited to a single lobe. In the remaining patient (Case 1) it was localized in the upper portion of the lung, which was devoid of any lobar architecture. The persistence of air leak in this case following local resection of the lesions and the development of residual lesions in the lower lobe of Case 5, following basal segmentectomy, support total lobectomy as the procedure of choice when possible. Case 3 is of particular note in that massive emphysema of the middle lobe had apparently prevented adequate inflation of the upper and lower lobes since birth. Whether the primary process here was emphysema or atelectasis is unknown, but the expansion permitted by thoracotomy was maintained and the excellent result lasting.

Three of the resected specimens contained typical bronchogenic cysts lined by the characteristic columnar-type bronchial epithelium. One resected lobe was found to consist almost entirely of multiloculated cysts having alveolar walls. Whether this represented rupture of alveoli secondary to trap-valve bronchial obstruction previously described or a primary defect in pulmonary parenchyma is a matter of conjecture. Case 1 is interesting in that this infant had an exploratory celiotomy in another hospital for suspected diaphragmatic hernia.

Summary and Conclusions

This experience with pulmonary and intrapleural tension phenomena, due to various causes in the infant and the newborn, defines a problem with distinct surgical indications. Quite a separate clinical entity is the incidentally discovered asymptomatic pulmonary cyst or the postinflammatory cavitary lesion, which has been known to close under favorable circumstances. The documented spontaneous disappearance of the latter cannot be taken to support expectant observation or conservative management of tension spaces in the lung or pleural cavity of the infant or the newborn. The limited respiratory reserve, increasing anoxia, and near-terminal exhaustion of these babies in their efforts to breathe make exploration mandatory. Thoracotomy permits immediate definitive correction of the process and is thus well tolerated.

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REFERENCES

1. Caffey, J.: On the Natural Regression of Pulmonary Cysts During Early Infancy, Pediatrics 11:48-63 (Jan.) 1953.

2. Cooke, F. N., and Blades, B.: Cystic Disease of the Lungs, J. Thoracic Surg. 23:546-569 (June) 1952.

3. Ehrenhaft, J. L., and Taber, R. E.: Progressive Infantile Emphysema: Surgical Emergency, Surgery 34:412-425 (Sept.) 1953.

4. Fischer, H. W.; Potts, W. J., and Hollinger, P. H.: Lobar Emphysema in Infants and Children, J. Pediat. 41:403-410 (Oct.) 1952.

5. Gross, R. E.: Congenital Cystic Lung: Sucfessful Pneumonectomy in a 3-Week-Old Baby, Ann. Surg. 123:229-237 (Feb.) 1946.

6. Gross, R. E., and Lewis, J. E., Jr.: Defect of the Anterior Mediastinum: Successful Surgical Repair, Surg. Gynec. & Obst. 80:549-554 (May) 1945.

7. Moersch, H. J., and Clagett, O. T.: Pulmonary Cysts, J. Thoracic Surg. 16:179-194 (April) 1947.

8. Ravitch, M. M., and Hardy, J. B.: Congenital Cystic Disease of the Lung in Infants and in Children, Arch. Surg. 59:1-36 (July) 1949.

9. Robertson, R., and James, E. S.: Congenital Lobar Emphysema, Pediatrics 8:795-804 (Dec.) 1951.

10. Schenck, S. G.: Congenital Cystic Disease of the Lungs: Clinicopathological Study, Am. J. Roentgenol. 35:604-629 (May) 1936.

11. Shaw, R. R.: Localized Hypertrophic Emphysema, Pediatrics 9:220-226 (Feb.) 1952.

Thyroid Carcinoma and Nodular Goiter in a Community Hospital

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Disagreement still continues as to the actual incidence of thyroid carcinoma in nodular goiter and, indeed, as to whether the two are truly related. Numerous investigators have reported series in which the incidence varies from 5% to as high as 17%.[1-4,7] These reports, however, have come from large medical centers, and the objection has been raised that selection has taken place before the patient arrives at such an institution, with the result that there is a higher proportion of goiters which are suspected of being malignant before operation. These figures, therefore, may not be representative of the occurrence of carcinoma in goitrous persons in the general population. This view is supported by a study carried out over a period of 25 years at the community level, in which in 379 thyroidectomies performed there was an incidence of carcinoma of 1.6%.[11] In an effort to cast further light upon the occurrence of thyroid cancer in patients brought to surgery in a community hospital, every thyroidectomy performed at the Ohio Valley General Hospital in the 27-year period from 1930 to 1956, inclusive, was reviewed.

Incidence of Carcinoma

The series consists of 1216 cases in which operation was performed for goiter; 879 of the goiters were adenomatous. No attempt was made to differentiate between toxic and nontoxic nodular goiter. There were 30 thyroid malignancies, 2.5% of the entire series (Table 1). Twenty-eight of these occurred in adenomatous glands, a rate of 3.4%. The other two malignancies were in cases of lymphomatous chronic thyroiditis (Hashimoto's disease). As shown in other series, malignancy was three times as common in the solitary adenoma as in a gland with multiple nodules, the incidences being 4.7% and 1.8%, respectively. The inaccuracy of clinical differentiation of the solitary adenoma and the multiple adenomatous goiter, brought out by Lange and MacLean,[8] was substantiated in this study. Many glands thought to contain only one adenoma preoperatively were found to have two or more at the time of operation. In the present series the term "solitary adenoma" refers to those glands found to have a single tumor by the operating surgeon and the pathologist.

In an effort to determine the prophylactic effect of thyroidectomy (as a cancer "preventive"), the series was divided into two groups: In the first period, from 1930 to 1944 inclusive, thyroidectomy was usually performed for reasons other than the prophylaxis or early detection of malignancy in the gland. In the second period, from 1945 to 1956, a more concerted effort was made to remove adenomatous glands, particularly when the adenoma was thought to be solitary (Table 2). Attention is brought to the fact that in the first period 39.2% of all glands removed were for diffuse toxic

TABLE 1.—*Carcinomas of Thyroid Gland in 1216 Thyroidectomies, 1930-1956*

	No. of Thyroidectomies	No. of Carcinomas	Percent Carcinomas
All cases	1216	30	2.5
All adenomatous goiters	879	28	3.4
Multiple adenomatous goiters	448	8	1.8
Solitary adenomas	431	20	4.7
Chronic thyroiditis	50	2	4.0

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TABLE 2.—*Analysis of 1216 Thyroidectomies*

	First Period (1930–1944)		Second Period (1945–1956)	
	No.	Percent	No.	Percent
Diffuse toxic goiter	149	39.2	138	16.5
Multiple adenomatous goiter	137	36.1	311	37.2
Solitary goiter	83	21.8	343	41.0
Chronic thyroiditis	6	1.6	44	5.3

goiter, whereas in the second period only 16.5% fell in this category. The proportion of multiple adenomatous glands removed was about the same, but in the second period the proportion of patients operated on for "solitary" adenomas doubled.

Table 3 shows the incidence of carcinoma in the various types of goiter in the two periods under study. It would be expected that many of the adenomatous goiters removed in the period from 1930 to 1944 were removed because of suspicion of malignancy, and that therefore in the period from 1945 to 1956, when there was a more concerted effort to remove this type of gland regardless of its clinical appearance, there would be a decrease in the percentage of malignancy in the latter group. It is to be seen that the percents of cancer are almost identical in both types of adenomatous goiter in the two periods. The rise in incidence of malignancy in all cases from 1.6% to 2.9% is explained by the increase in the relative number of adenomatous glands removed in this second period as compared with the number of diffuse toxic goiters. This might give the impression that extending the indications for removing adenomatous goiters, both those with multiple and those with solitary nodules, resulted in the recognition of thyroid cancer in a higher proportion of cases. However, when we exclude those cases in the second period whose first manifestation of disease was cervical metastasis, the increase is less marked. There were no cases of carcinoma with cervical metastases in the first time period. In seven of the patients in the second group a diagnosis of malignancy was made preoperatively by the clinical finding of spread to the lymph nodes of the neck. When these seven cases are excluded (Table 3), the incidence of carcinoma in solitary nodules is lowered to 3.8% and in multiple adenomatous goiters to 0.7%. Only 2.3% of all adenomatous glands in this group were found to contain carcinoma. If one excludes in addition cases in which the preoperative diagnosis was cancer, the incidence of cancer in the remaining cases is cut even more. By comparison with series from larger institutions, Horn and Dull,[7] covering essentially the same period of time, reported an incidence of 7.1% of carcinoma in all adenomatous glands removed at the Hospital of the University of Pennsylvania.

These findings are compared with those reported by other investigators in Table 4. A high incidence of thyroid carcinoma is

TABLE 4.—*Comparison of Present Series with Reports in the Literature*

Series	Nodular Goiter	Carcinoma in Nodular Goiter, %	Carcinoma in Solitary Adenomas, %
Horn and Dull (Univ. Pennsylvania)	2638	8.9	...
Crile (Cleveland Clinic)	537	5.6	24.5
Cole	663	8.0	24.4
Ochsner Clinic	580	8.8	19.8
Crabtree and Hunter (Univ. of Michigan)	1435	9.0	24.3
Watt and Foushee	214	1.7	2.5
Hershey	879	3.4	4.7

TABLE 3.—*Comparative Incidence of Thyroid Carcinoma in Two Periods of Study*

	First Period (1930–1944)			Second Period (1945–1956)					
				All Cases			Cases Without Metastasis		
	No.	Carcinoma	% Carcinoma	No.	Carcinoma	% Carcinoma	No.*	Carcinoma	% Carcinoma
All cases	380	6	1.6	836	24	2.9	829 (7)	17	2.1
All adenomatous goiters	220	6	3.4	654	22	3.4	647 (7)	15	2.3
Multiple adenomatous goiters	137	2	1.8	311	6	1.9	307 (4)	2	0.7
Solitary adenoma	83	4	4.7	343	16	4.7	340 (3)	13	3.8
Chronic thyroiditis	6	0	0.0	44	2	4.6	44 (0)	2	4.6

* Numbers in parentheses indicate cases in which preoperative diagnosis of malignancy was made on the basis of cervical metastasis.

TABLE 5.—*Percentage Incidence of Carcinoma by Sex*

	All Cases	Multiple	Solitary
Male	7.0%	10.5% (4 of 38)	14% (7 of 50)
Female	1.8%	1.2% (5 of 410)	3.4% (13 of 381)

seen in the large medical centers. Watt and Foushee [11] report a low incidence in a community hospital in southwestern Georgia.

As stated earlier, no attempt has been made to separate the toxic and the nontoxic nodular goiters in the present series. It has been pointed out by many that the incidence of carcinoma in toxic nodular glands is very low. Cole and associates,[3] for instance, report an incidence of carcinoma of 1% in toxic nodular goiter, but of 17% when toxicity was not present. This marked discrepancy must be a result of the surgical indications in the two groups. The patient with a toxic nodular goiter has an operation because of the toxicity present, not because of suspicion of malignancy. The nontoxic patient is referred because of suspicion of malignancy or pressure symptoms, or for cosmetic reasons.

Age and Sex

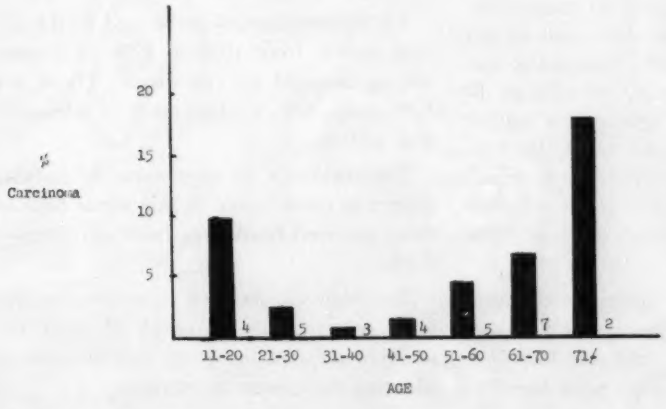
Male patients made up 13% of the series, yet were found to have 36.7% of the malignancies. In all patients undergoing thyroidectomy (both diffuse and nodular goiters), carcinoma was found in 7% of the male patients but in only 1.8% of the female patients (Table 5). In the male patients, 10.5% of multiple adenomatous goiters and 14% of solitary adenomas were malignant, as compared with 1.2% and 3.4%, respectively, in the female patients. It is in the male group of patients, therefore, that our figures more closely approach those from larger centers.

The accompanying graph covers the age distribution in this series. The high incidence of carcinoma in nodular goiter in children and adolescents has been pointed out by numerous authors; the incidence of 9.9% of malignancy in patients between the ages of 11 and 20 in this series is consistent with this observation. Of the four patients in this age group with thyroid carcinoma, three had cervical metastases at the time of first examination. The incidence of carcinoma is quite low in the age group of 21 to 50, but begins to rise again after the age of 50.

There was very little difference in the average age of all the patients with goiters as compared with that of patients with carcinomas, being 42 and 45 years, respectively. The average duration of the tumor was found to be exactly the same in patients with adenomatous goiters and in those with carcinoma, namely eight years.

Comment

The figures here reported show an incidence of carcinoma of 2.5% in all goiters



Percentage of carcinoma by age groups. The number of cases is represented by the figure beside the column.

and of 3.4% in adenomatous goiters, rates much lower than those reported by most authors. The patients in this study lived within a radius of 50 miles in the states of West Virginia, Ohio, and Pennsylvania. Although some patients with thyroid malignancy undoubtedly have gone outside the area for treatment, it is doubtful whether this factor affects the figures in any significant degree. Actually, the cross section of patients reported here should be more representative of the general population than those treated at the large metropolitan centers reporting a much higher incidence of carcinoma. Despite a considerable increase in the number of adenomatous goiters removed in the second time period, it should be emphasized that it has not been the policy to resect all thyroid lesions. Sokal[10] has pointed out that many internists and general practitioners will refer the patient to a surgeon only if they believe that there is a serious risk of malignancy in a goiter, but will otherwise hold the patient or refer him to a surgeon not likely to recommend a needless operation. This factor of selection, however, would hardly account for the degree of difference between this series and others.

The histopathological interpretation of thyroid malignancy is difficult and controversial, as pointed up by the very interesting study by Perloff and Schneeberg.[9] They sent slides on 30 previously diagnosed cases of primary carcinoma to seven of the leading thyroid pathologists in the country. In 13 cases all agreed completely in their diagnoses, and in an additional 6 cases all but one pathologist concurred. Substantial disagreement existed, however, in at least 10 of the cases. When the figures were revised on the basis of the opinions of the consultant pathologists, the incidence of carcinoma in nontoxic nodular goiter in their series was significantly lowered from 5.2% to 3.2%.

Our most significant finding is the high incidence of thyroid carcinoma in the male —14% of solitary adenomas and 10.5% of multiple adenomatous goiters were found to be malignant in the male, as compared with 3.4% and 1.2% in the female. From these figures the conclusion must be drawn that all adenomatous goiters in the male patients should be looked upon with suspicion, and the policy of removal of all such glands appears justified. The incidence of 3.4% in solitary adenomas in the female patients would also appear to justify the same policy, since this type of lesion is easily removed and the procedure should be accompanied with no mortality and little morbidity. The extremely low figure of 1.2% (only 5 carcinomas found in 410 multiple adenomatous goiters) would raise some doubt as to the justification of such a policy in the female in regard to multiple adenomas. Significantly, female patients with multiple nodular goiters made up 47% of the cases with adenomatous lesions in this series.

The high incidence of malignancy in nodular goiters in childhood and adolescence is substantiated in this study, and the removal of all nodular goiters in this group should be advocated. Between the ages of 30 and 50 the incidence of malignancy was found to be approximately 1%, but there was a sharp rise after the age of 50. Of the 13 patients with thyroid malignancy over 50 years of age, 5 had noticed a goiter before they had reached that age and the remaining 8 were not cognizant of its presence until after the age of 50.

Summary

All thyroidectomies performed in the 27-year period from 1930 to 1956 in a community hospital are reviewed. There are 1215 cases, 879 of which were of adenomatous goiters.

The incidence of carcinoma in nodular goiters is much lower in this series than in those reported from large medical centers—3.4%.

The high incidence of carcinoma in the male warrants the removal of both the multiple adenomatous goiter and the solitary adenoma for cancer prophylaxis.

In the female, removal of the solitary adenoma is advisable, but justification for the policy of resection of all adenomatous goiters is not so clear because of the very infrequent occurrence of malignancy in this group.

Thyroidectomy for possible malignancy is advisable in adenomatous goiters in infants and children.

The Wheeling Clinic.

REFERENCES

1. Cerise, E. J.; Randall, S., and Ochsner, A.: Carcinoma of the Thyroid and Nontoxic Nodular Goiter, Surgery 31:552 (April) 1952.

2. Cole, W. H.; Slaughter, D. P., and Rossiter, L. J.: Potential Danger of Nontoxic Nodular Goiter, J. A. M. A. 127:883 (April 7) 1945.

3. Cole, W. H.; Slaughter, D. P., and Majarakis, J. D.: Carcinoma of the Thyroid Gland, Surg. Gynec. & Obst. 89:349 (Sept.) 1949.

4. Crabtree, H. N., and Hunter, D. C., Jr.: Carcinoma of the Thyroid: Clinicopathologic Study, A. M. A. Arch. Surg. 67:175 (Aug.) 1953.

5. Crile, G., Jr., and Hazard, J. B.: Relationship of the Age of the Patient to the Natural History and Prognosis of Carcinoma of the Thyroid, Ann. Surg. 138:33 (July) 1953.

6. Crile, G., Jr., and Dempsey, W. S.: Indication for Removal of Nontoxic Nodular Goiter, J. A. M. A. 139:1247 (April 30) 1949.

7. Horn, R. C., Jr., and Dull, J. A.: Carcinoma of the Thyroid: A Re-Evaluation, Ann. Surg. 139: 35 (Jan.) 1954.

8. Lange, H. J., and MacLean, K. F.: Malignant Neoplasms of the Thyroid, Surgery 26:862 (Nov.) 1949.

9. Perloff, W. H., and Schneeberg, N. G.: The Problem of Thyroid Carcinoma, Surgery 29: 572 (April) 1951.

10. Sokal, J. E.: Surgical Statistics on Malignant Goiter, Surg. Gynec. & Obst. 99:108 (July) 1954.

11. Watt, C. H., and Foushee, J. C.: The Incidence of Carcinoma in Nodular Thyroids in Southwest Georgia, J. M. A. Georgia 40:414 (Oct.) 1951.

Obstruction of the Small Intestine Caused by Acute Cholecystitis

Report of a Case

GEORGE L. HOFFMANN Jr., M.D.; KLAUS F. L. von KESSEL, M.D., and STANLEY O. HOERR, M.D., Cleveland

Obstruction of the small bowel resulting from an acute inflammation of the gallbladder is rare. Blain and Harkins [1] studied reports of 11,794 operations and 19,274 necropsies and found 41 cases of perforated gallbladder. In 11 cases there was associated intestinal obstruction; however, only 4 cases presented as obstruction, and in 2 of those the obstruction was a gallstone ileus. Their series did not include the intact, nonperforated, acutely inflamed gallbladder. Nemir,[2] in his study of 430 cases treated during a 10-year period at the Hospital of the University of Pennsylvania, describes no case similar to the one we are reporting. Furthermore, in a search of the indexed literature for the past 17 years no published case report was found. Analysis of the Cleveland Clinic records indicates that the case to be reported is the first such case seen here, in which the only complaints and findings are related to acute obstruction of the ileum.

Report of Case

A 64-year-old Negro garage superintendent was admitted on May 21, 1957, with the chief complaint of vomiting of seven day's duration. For about three months prior to admission the patient had noted some anorexia; yet he specifically asserted that he had no intolerance to fatty foods, no colicky pains in the epigastrium or right upper quadrant, no jaundice, no light stools or dark urine. In the last month prior to admission, he experienced some mild intermittent pain in the right lower quadrant, although the bowels were regular until the last week. He had lost about 10 lb. in weight. He had had no abdominal operations.

On the sixth day before admission, while driving to work, the patient had a sudden onset of pain in the lower abdomen, which was soon followed by the vomiting of copious amounts of light-green material and by diarrhea; thereafter he was unable to retain food. The diarrhea persisted for four days; for two days before admission he passed no stool or gas.

Examination revealed a well-developed, obese, dehydrated Negro man, who appeared acutely ill. The abdomen was greatly distended, and there were slight diffuse tenderness and tympany. No

Fig. 1.—X-ray on admission, showing small-bowel obstruction.

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From the Department of General Surgery, The Cleveland Clinic Foundation, and The Frank E. Bunts Educational Institute.

Chief Resident of a General Surgical Service, Cleveland Clinic Hospital (Dr. Hoffmann). Resident in the Department of General Surgery, The Cleveland Clinic Foundation (Dr. von Kessel).

Fig. 2.—Sketch of the inflamed gallbladder causing ileal obstruction.

masses were palpable, and the rectal findings were negative except for moderate prostatic enlargement. Roentgen findings confirmed the clinical impression of obstruction of the small bowel (Fig. 1). A barium roentgen examination of the colon, given shortly after admission, showed no abnormal findings. Therapy consisting of intestinal intubation and intravenous feedings was begun. During the first 12 hours the intestinal drainage exceeded 5000 ml. of green, watery material. Because the patient's condition failed to improve after 48 hours of conservative therapy, and on the basis of a preoperative diagnosis of small-bowel obstruction, probably from tumor, an exploratory laparotomy was performed.

Under endotracheal anesthesia, the abdomen was opened by a lower right rectus incision, which later was extended up to the xiphoid via the midline. Approximately 3 ft. above the ileocecal valve the ileum was adherent to the acutely inflamed gallbladder, and the kinking at that point (Fig. 2) produced the obstruction. By blunt dissection the bowel was separated from the inflammatory mass and a cholecystectomy was performed; the common duct was not explored. The gallbladder bed was drained, and the abdomen was closed. Postoperatively the abdomen remained distended for several days because of a rather troublesome ileus, which subsequently responded to conservative measures. The patient was discharged on the 18th postoperative day.

Pathologic examination of the gallbladder revealed that it contained innumerable tiny, faceted stones, and microscopic findings were compatible with acute cholecystitis.

Summary

A unique case of acute cholecystitis in a 64-year-old Negro man is reported in which the presenting signs and symptoms were due to a secondary small-bowel obstruction produced by a loop of terminal ileum caught up in the inflammatory process surrounding the intact gallbladder. Search of recent literature and hospital records fails to reveal a similar case report.

Cleveland Clinic, 2020 E. 93d St. (Dr. Hoerr).

REFERENCES

1. Blain, A., and Harkins, H. N.: Intestinal Obstruction Due to Perforations of the Gall Bladder, Surgery 21:110-135 (Jan.) 1947.

2. Nemir, P., Jr.: Intestinal Obstruction: Ten-Year Statistical Survey at the Hospital of the University of Pennsylvania, Ann. Surg. 135:367-375 (March) 1952.

Instrument to Assist in the Surgical Removal of Stones from the Bile Ducts

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The importance of following a sound surgical technique for exploring the bile ducts and removing contained stones has recently been stressed by Allen [1] and by Welch,[2] and both authors have ably described and illustrated such procedures. Of the various instruments used for these operations, each has its limitations and usually leaves something to be desired.

Stones in the common bile duct may be removed with scoop or forceps, or, at times, fragmented and either irrigated out or forced through into the duodenum after dilatation of the sphincter of Oddi, not always a gentle or safe procedure. Calculi in the common hepatic duct present a greater problem, for any instrumentation may force the stone up into the right or left hepatic duct, and removal with a scoop or forceps may be difficult or impossible. Some surgeons feel that if the sphincter of Oddi is adequately dilated at operation, residual calculi in the hepatic ducts will later pass into the duodenum, but how much surer and more satisfying it is to the surgeon to remove them at the time of operation!

To aid in cleansing the bile ducts of foreign matter, we considered using various sizes of suction bells, attached to thin, malleable metallic suction tubing, so that, as the instrument is advanced in the duct, the bell part might trap calculi, where they could be held by suction and removed as the instrument was withdrawn prior to reinsertion. It was also felt that it would be easy to irrigate a duct with such an instrument, removing small calculi or debris by alternate irrigation and suction.

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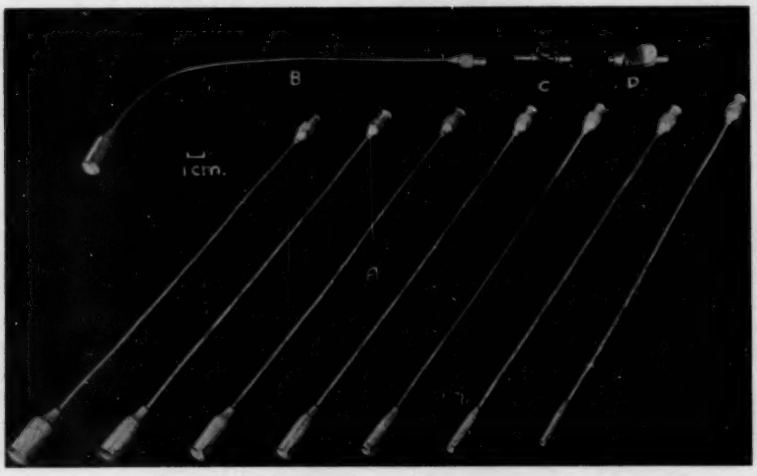
From the Department of Surgery, Nazareth Hospital.

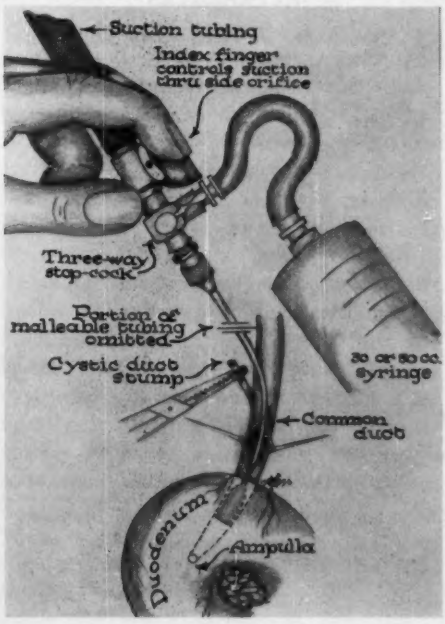
Fig. 1.—*A*, graduated sizes of suction bells in the set. Each is 23 cm. long. *B*, malleable tubing molded with the fingers to avoid kinks and to conform to duct anatomy. *C*, three-way stopcock. *D*, adapter with side-orifice to connect to operating-room suction tubing.



These metal bells have been made up in various diameters (Fig. 1), corresponding to the sizes of Bakes dilators, and each is attached to a 23 cm. length of malleable metal tubing. At the end of each tube opposite the bell, a standard needle hub is affixed. Accessory pieces are a three-way stopcock to allow for irrigation, and an adapter with a side-opening by which to attach the stopcock to the rubber tubing of the operating-room suction equipment. The side-opening permits control of suction by using intermittent finger pressure over the orifice (Fig. 2). The stopcock also aids in flushing debris out of the suction bell after it has been removed from the bile duct.

A bell of appropriate size to fit into the duct of the patient is selected, and the tubing curved gently in the fingers to adjust to the direction of the duct, care being taken to avoid kinking. After connecting the three parts of the instrument in series, with the adapter inserted into the rubber suction tube, the bell can be inserted into the bile duct through a previously made incision in the duct wall, which is held open by guy sutures. While the bell is advanced in the duct, the side-hole in the adapter is left open so that there is no suction on the bell during insertion. As the instrument is withdrawn, intermittent or continuous suction can be used on the bell by finger pressure over the side-opening of the adapter (Fig. 2). Alternate irrigation and suction can be used through the three-way stopcock, with the operator controlling the valve and suction and the assistant using the syringe containing sterile saline or water.

Fig. 2.—Diagram to illustrate use of the instrument in the bile duct. The operator manipulates the suction bell and stopcock, while the assistant handles the syringe.



Repeated insertions and withdrawals of the bell for varying distances and in both directions may be needed, with or without irrigation to remove multiple small stones or debris. The edges of the bells are smooth and, if judiciously used, will not damage the duct lining. Foreign material trapped in the bell can be flushed out after removal of the instrument from the duct.

It should be emphasized that these bells are designed only as accessory instruments, and are not intended to replace any instruments currently used in common-duct surgery. Most important, they are not designed as probes or dilators and should not be used as such.

These instruments have been available to us since Jan. 1, 1956, and in the 20 months between that date and Sept. 1, 1957, operation has been performed on 133 patients with calculous cholecystitis. Sixty-five of these patients (48.8%) had cholecystectomy without common-duct exploration or operative cholangiography.*

One of us (P. R. C.) began using operative cholangiography early in 1956, and in 28 patients without indication for common-duct exploration, operative cholangiography via the cystic duct was done. All these x-ray studies were negative, and none gave information which prompted choledochostomy.

* About 40% of the group of 133 patients had an incidental appendectomy.

In 40 patients cholecystectomy and common-duct exploration were done, the indications for choledochostomy in each instance being the standard ones familiar to most surgeons. Of this group, stones were removed from the common ducts of 19 patients (47.5%). After completion of duct exploration, removal of stones, and insertion of a T-tube in each patient, 39 of the group were studied with operative cholangiography (17 instances) or postoperative cholangiography (22 instances), the latter examinations being carried out 8 to 10 days later. All 39 cholangiograms were negative.

Of the 40 patients upon whom choledochostomy was done, one did not have a subsequent cholangiogram. She was a 74-year-old woman admitted with severe diabetes, acute calculous cholecystitis, and cholangitis. At the time of operation an acutely inflamed gallbladder containing numerous stones was removed, and the common duct was found to be dilated and packed tightly with granular debris. Culture of the common duct yielded Klebsiella pneumoniae. The duct was cleaned out and a T-tube inserted. Postoperatively, in spite of reasonable fluid intake and diabetic control, her urinary and bile output remained extremely small, and she died on the ninth postoperative day. At autopsy she was found to have advanced nephrosclerosis, portal vein thrombosis, and a residual gallstone, 6×8 mm. in diameter, pocketed in a diverticulum arising from the lower end of the common duct.

There was one other death in this group of patients, that being of a 71-year-old woman with diabetes, poor cardiac reserve, and acute calculous cholecystitis. She died of pulmonary emboli one day after cholecystectomy done under local anesthesia.

The over-all mortality for the 133 patients was 1.5%, and, as far as we can now determine, one residual common-duct stone occurred in 40 patients whose common ducts were explored.

The common-duct suction bells were used along with Bakes dilators in each choledochostomy and were of great help in removing calculi, particularly from the hepatic ducts.

It is of interest that the bells were of help on the urologic service in removing small stones from the renal pelvis at the time of nephrostomy.

This instrument is available from Mr. Paul Gilson, surgical supplies dealer, 5663 Ogontz Ave., Philadelphia 41.

6833 Castor Ave. (49).

REFERENCES

1. Allen, A. W.: A Technique for Choledochostomy, A. M. A. Arch. Surg. 72:532 (March) 1956.

2. Welch, C. E.: Choledochotomy, Surg. Gynec. & Obst. 102:495 (April) 1956.

Stricture of the Trachea Following Traumatic Fracture

Successful Excision and Anastomosis

JULIAN K. QUATTLEBAUM Jr., M.D., Savannah, Ga.

Rupture of the intrathoracic trachea and bronchi is now a well-recognized complication of nonpenetrating injuries of the chest. The usual pattern of injury has been described by Kinsella and Johnsrud [1] and confirmed by Mahaffey and associates,[2] who have accumulated numerous references to indicate that the region of the tracheal bifurcation is the most susceptible site in the respiratory tract to the force of a severe crushing chest injury. Rupture of one of the major bronchi with or without extension proximally into the trachea or distally into the secondary bronchi is the common result. It would seem that rupture of the trachea alone is a much less common occurrence, although it is possible that small rents in the trachea occur more frequently than is generally recognized and go on to heal spontaneously.[3] In the trachea the rupture may take the form of an irregular longitudinal tear,[4-6] or of a transverse fracture.[1,7] There may occur separate simultaneous ruptures of the trachea and of the bronchi.[5,6] The common late complication of transverse fractures of the major air passages is cicatricial stenosis. An excellent recent review of such injuries to the major bronchi serves to emphasize this point.[2] Stenosis of the more cephalad portion of the thoracic trachea secondary to chronic inflammatory disease has been reported by Bikfalvi and Kassay,[8] who deserve recognition for the first successful resection of a stricture of the intrathoracic trachea with end-to-end anastomosis. Richards and Cohn [7] resected a traumatic stricture 2 cm. above the carina, but found it necessary to splint the anastomosis with an indwelling tracheotomy tube because of restenosis. After 18 months the plastic tube was removed. The trachea has subsequently remained open, allowing the patient to pursue a gainful occupation.[9] These authors have emphasized the difficulties of late repair and hence the importance of early recognition of the injury. Because stenosis secondary to isolated rupture of the trachea well above the carina has hitherto been unreported, and because this case represents the third successful attempt at surgical correction of circumferential stenosis of the intrathoracic trachea, it is here reported.

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From the Department of Surgery, The Johns Hopkins School of Medicine and The Johns Hopkins Hospital, Baltimore.

Report of a Case

A 22-year-old Negro man was first admitted to the Northampton-Accomack Memorial Hospital, in Nassawadox, Va., on June 19, 1956, shortly after having driven his automobile into a telephone pole to avoid head-on collision with a truck. He could not recall other details of the accident. He was found to have lacerations of the nose and the left eye globe and had mild concussion. There was x-ray evidence of mediastinal emphysema and partial left pneumothorax (Fig. 1). The eye and nose wounds were sutured. No specific therapy was directed to the thorax. His lacerations healed uneventfully, and his course was otherwise uncomplicated. He was discharged July 2, but was readmitted seven days later because of pain in the left eye and loss of vision. Enucleation of the left eye was carried out on July 15, under thiopental (Pentothal) sodium anesthesia, without incident.

On July 17, severe paroxysms of coughing were noted, and there was obvious air hunger. The following day the asthmatic type of breathing was evident, and his respiratory distress became gradually severer, with inspiratory as well as expiratory stridor. On July 20 a tracheotomy was performed, and his distress was partially re-

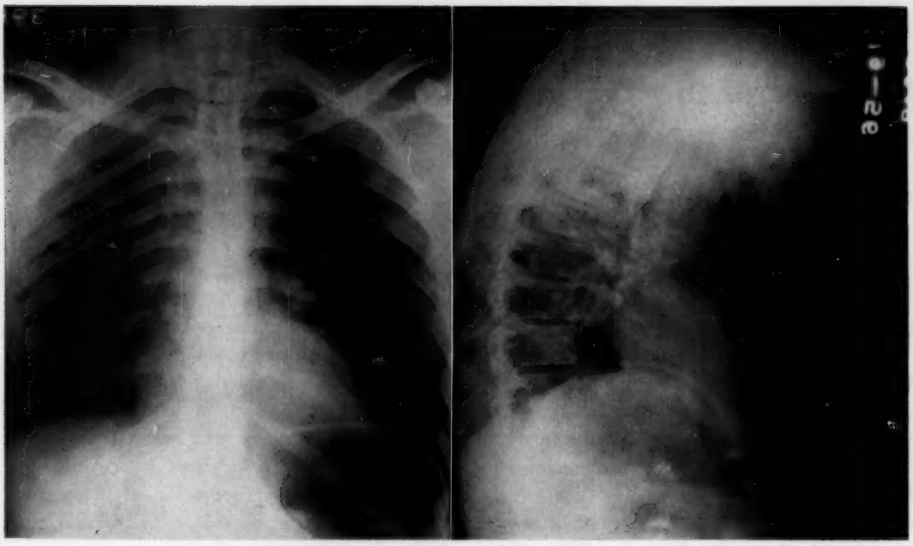

Fig. 1.—Chest x-ray taken on day of original injury, showing extensive mediastinal emphysema extending into neck as well as small left pneumothorax.

lieved. He was able to be up and about until July 26, when respiratory obstruction again became severe, in spite of the tracheotomy. Bronchoscopy was carried out, and severe stenosis of the trachea below the level of the sternal notch was noted. A No. 21 F. endotracheal tube was the largest that could be passed through the stenotic area. With introduction of this tube, the air hunger was completely relieved, and the patient became quite comfortable.

He was transferred by ambulance to The Johns Hopkins Hospital on July 27. On admission to the emergency ward, he was seen to be a slender, young Negro man who was in no acute distress, and who was breathing quite comfortably through a small rubber catheter which issued from a tracheotomy incision in the anterior portion of the neck. There was evidence of moderate dehydration. The left eye was absent. Otherwise the examination was essentially negative. Breath sounds were well heard on both sides and were normal. Chest x-ray showed the lungs to be well expanded, without infiltration, and the endotracheal catheter could be seen extending into the right main bronchus. The area of stenosis could not be definitely outlined, but appeared to be at the level of the fourth posterior intercostal space. The hemoglobin was 17 gm. per 100 cc., the white blood cell count 13,400 per cubic millimeter. The urine had a specific gravity of 1.020, with acid reaction and with no albumin or sugar. Microscopic examination of a centrifuged specimen showed 2 or 3 white cells per high-power field.

Because of the precarious airway, it was elected not to introduce dye to outline the stricture. After a brief period of hydration the patient was taken to the operating room for exploratory thoracotomy. Anesthesia was administered by Dr. Donald Benson, being induced with cyclopropane through the indwelling tracheal catheter. Positive-pressure assistance was provided until the chest was opened, after which positive-negative respiration was maintained with the Jefferson respirator. A standard posterolateral thoracotomy was performed, the fifth rib being resected, as well as a short segment of the posterior fourth rib. Exposure was good. A solid block of dense scar containing small areas of calcification was found to occupy the mediastinum from the level of the thoracic inlet to the superior border of the azygos vein, and extending from the vertebral column, behind, to the posterior aspect of the superior vena cava, in front. Dissection was difficult and tedious. Ultimately the trachea was freed from the adherent esophagus, ascending aortic arch, and innominate artery, and then was mobilized into the neck. The right vagus nerve was dissected out of the scar and preserved, and its recurrent laryngeal branch was seen to be intact as it coursed about the subclavian artery. Posteriorly the esophagus was seen to be markedly constricted and held against the vertebral column by the dense cicatrix. A longitudinal incision was made in its scarred muscularis anteriorly for about 6 cm., allowing the mucosa to pout out.

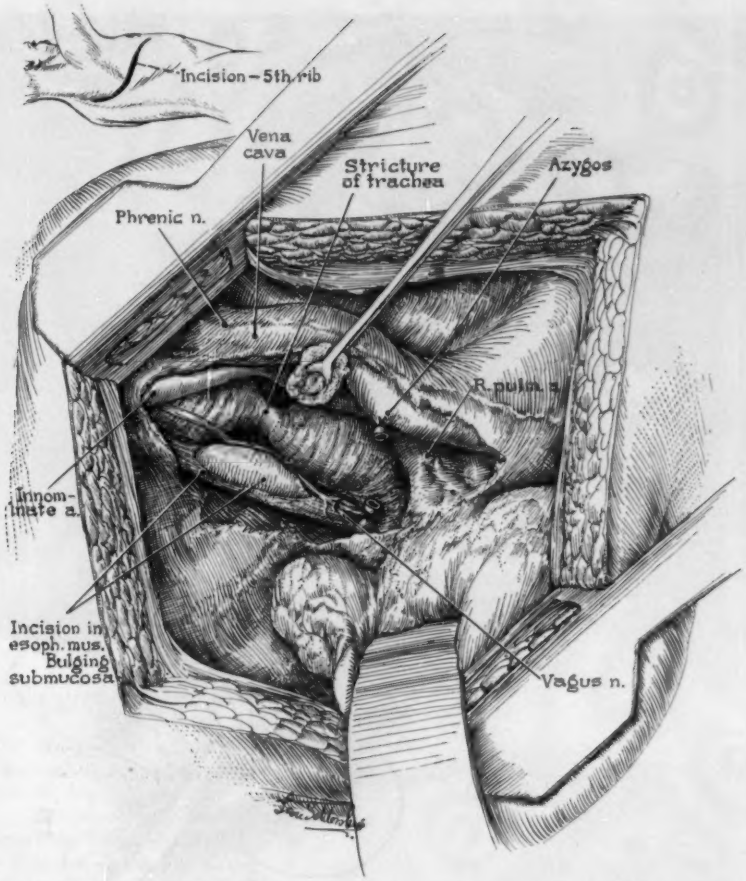

Fig. 2.—Sketch showing findings at operation. For purposes of clarity, the residual mediastinal scar has not been shown.

As the trachea was freed, it was seen that there existed a severe hourglass type of stenosis over a 1.0 to 1.5 cm. length, with the lower border approximately 4.0 cm. above the carina. It appeared as though there had been a complete transverse fracture of the trachea with retraction of the edges, allowing the intervening space to be filled in with scar tissue (Fig. 2). The lower segment was offset to the right, less than 1.0 cm. but enough that the distal portion of the trachea was no longer in direct alignment with the proximal portion. The scar causing the stenosis was excised in a wedge, leaving a 1.0 cm. hinge along the left border of the strictured segment. This allowed control over the trachea while the small catheter was replaced with a No. 32 F. endotracheal tube, which was passed through the larynx and down into the distal tracheal segment. Adequate ventilation was maintained by intermittent positive pressure in spite of considerable loss of gasses around the tube. With the hinge left on the left border, the remaining circumferences of the proximal and distal segments were approximated with interrupted figure-of-eight mattress sutures of 00 black silk, neither everting nor inverting the tracheal margins. An attempt was made to place the sutures through the full thickness of the tracheal wall except for the mucosa, thus avoiding exposure of the silk to the tracheal lumen (Fig. 3). Despite an original retraction of some 3.0 cm. along the right border as the stricture was excised, the two segments were approximated with remarkable ease, and there was no air leak from the suture line with forceful insufflation. Because of some residual offset of proximal and distal segments along the left border,

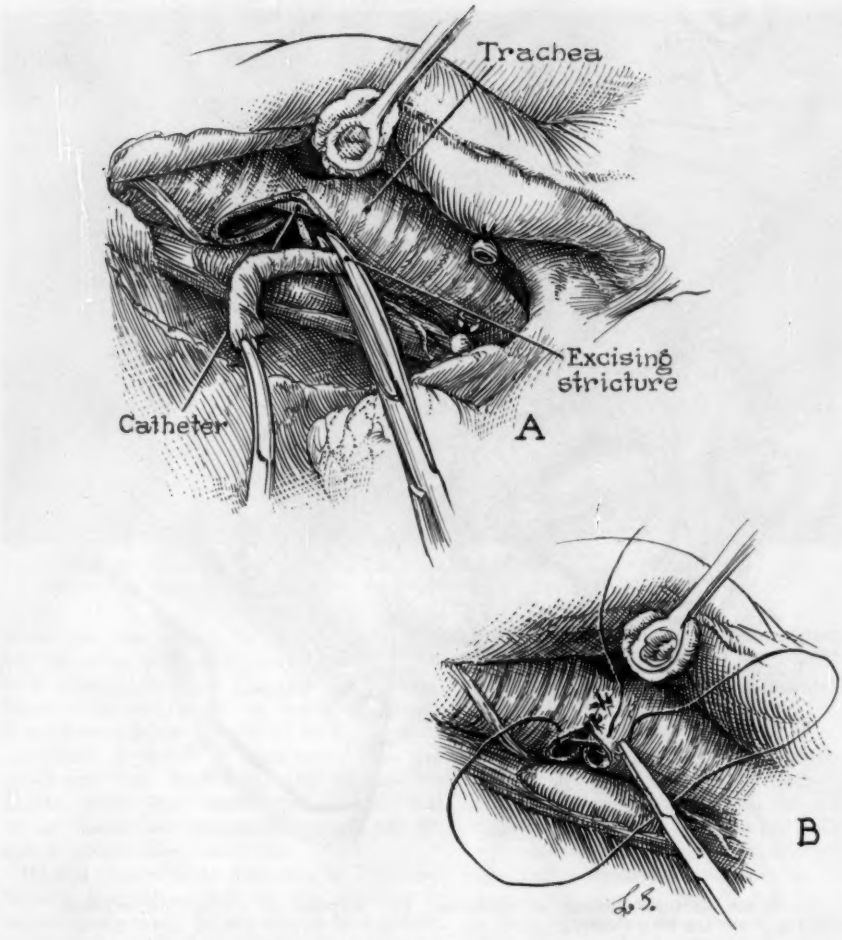

Fig. 3.—Excision of the stricture and anastomosis. Silk sutures do not penetrate through full thickness of the wall.

which had been left hinged, it was estimated that approximately three-fourths of the original tracheal lumen had been restored. Because of the scarring, no normal tissue remained with which to reinforce the anastomosis. The chest was closed, with two intercostal catheters in place for pleural drainage. A standard tube was inserted into the previous tracheotomy as the patient was extubated.

The postoperative course was complicated only by the necessity of evacuating an uninfected hematoma from the wound on the 17th postoperative day. The patient was able to breathe without difficulty from the outset, and he was not significantly febrile. The lungs remained well expanded, and the tracheotomy tube was removed on the 14th postoperative day. On the 18th day a glass-ball implantation in the left orbit was carried out, with local anesthesia, in preparation for a later prosthesis. On the 24th postoperative day laryngoscopy and tracheoscopy were carried out. The tracheal suture line was healing cleanly, without granulations or visible suture material. There appeared to be a shelf projecting inward from the left anterior aspect, reducing the tracheal lumen to approximately one-half its normal diameter. In addition, it was discovered that there existed a healed fracture of the right ala of the laryngeal cartilage, as well as a bilateral vocal cord palsy. The glottic aperture was estimated at 2.0 to 4.0 mm.

Serious consideration was given to the reestablishment of the tracheotomy, but in the absence of

Fig. 4.—Tracheograms made Sept. 26, 1956 (left) and June 5, 1957 (right), showing residual shelving of trachea at site of stricture. There has been no reduction in lumen during the eight months' interval.

obstructive symptoms this was deferred. The patient was discharged asymptomatic and fully ambulatory on Aug. 23, 1956, the 27th postoperative day, to be followed in Nassawadox, Va. He has subsequently been readmitted to The Johns Hopkins Hospital on three occasions for evaluation of his progress by laryngotracheoscopy and tracheography (Fig. 4). There has been no tendency toward further narrowing of the trachea in the region of anastomosis in the 10 months since operation. Beginning motion of the right vocal cord was noted on Sept. 24, 1956, and full range of motion was seen on Jan. 4, 1957. At this latter time pulmonary function studies showed a vital capacity of 4482 cc., a maximal breathing capacity of 101 liters per minute, and a maximum mid-expiratory flow rate of 2.58 liters per second. These figures are above the patient's predicted normal except for the maximal breathing capacity, which was approximately 80%. In June, 1957, left vocal cord palsy persisted. The patient has been gainfully employed in his usual occupation as a waiter and cook since October, 1956, and has gained some 15 lb. since discharge.

Comment

The mechanism of rupture of the trachea and bronchi with crushing injuries of the chest was described by Kinsella and Johnsrud [1] as some sort of shearing force being applied to the region of the carina. This explanation has been generally accepted by those writing on the subject, the force usually being considered as intratracheal and intrabronchial pressures transmitted by the force of the blow against a closed glottis, with rupture occurring in the theoretically weak region of the carina. Divarication of the pulmonary hili [10] and direct compression against the vertebral column [11] have also been proposed. Since transverse fracture of the bronchus and transverse fracture of the trachea in the thorax are similar to the complete transverse fractures of the trachea in the neck, such as those reported by Shaw [12] and by Fox,[13] the latter of which was certainly the result of a direct blow, it seems not unlikely that such intrathoracic injuries may actually be due to direct compression of the tracheobronchial tree against the vertebral column by the sternum or chest wall. Such an occurrence

is not inconceivable when one considers the forces usually involved and the fact that the same "shearing force" on occasions causes rupture of neighboring structures, such as the heart and aorta.[1] On the other hand, irregular tears of the type reported by Laurier, Messier, and Venne[4]; Thompson and Eaton,[5] and Dark and Jewsbury[6] would seem more likely to be produced by increased pressure within the major air passages. Probably a combination of factors is present in most tracheobronchial ruptures.

The clinical picture following rupture of the trachea or bronchus has been amply described.[7] The signs are related to bleeding and air leak at the site of rupture and express themselves as hemoptysis, pneumothorax, and mediastinal and subcutaneous emphysema. The presence and degree of each depends on the degree and the site of rupture and the degree of overlying pleural tear. Concomitant injury to surrounding structures may further complicate the clinical picture. The characteristic finding which should lead to prompt diagnosis is progressive, uncontrolled tension pneumothorax which fails to yield to catheter aspiration. However, in many cases this striking picture does not obtain, and at least in one case none of the usual signs was present.[2] The early diagnosis of tracheobronchial rupture must not then await the characteristic picture of massive air leak but, rather, must reside in the awareness of its possibility in any patient who presents with a history of chest trauma and who exhibits any one of the three major clinical signs, i. e., hemoptysis, pneumothorax, or mediastinal or subcutaneous emphysema. Once the diagnosis is suspected, bronchoscopy affords the method of choice for confirmation. Not only the presence and extent of rupture but also its site may be determined, and early surgical intervention may be carried out. This is infinitely preferable to late surgical therapy and will prevent deaths from delay and from increased technical difficulty.

The above case, remarkably similar in clinical course and operative findings to that of Richards and Cohn,[7] serves again to illustrate the difficulties of late surgical treatment. Dense mediastinal scarring not only made the dissection extremely difficult but also had produced marked compression of the esophagus. The history of delayed onset of laryngeal stridor, which barely preceded the subsequent severe tracheal obstruction, suggests that the vocal cord palsy may have occurred with maturation of mediastinal scar involving the recurrent laryngeal branches of the vagus nerve, although this cannot be established with certainty in view of the healing laryngeal fracture almost surely incurred at the time of the chest injury. The lack of complications of this nature following early repair of tracheobronchial rupture[4-6,14] suggests at least that they may be thus avoidable.

The leaving of a hinge of scar tissue on the left border of the tracheal anastomosis in this case was, in retrospect, unwise. The tracheal lumen was compromised from the outset, and only by good fortune was there no significant further stenosis at the anastomosis. The preliminary placement of one or two stay sutures would have served the function of this hinge and allowed full restoration of the tracheal lumen.

The question of suture materials seems less important. Silk has been used satisfactorily in many bronchial anastomoses and was satisfactory here. Troublesome granulations sometimes noted with silk may have been avoided by not leaving the suture material exposed to contaminated tracheal secretions. A method of accomplishing this same end by everting cuff closure has been described in experimental work by Jackson, Lefkin, Tuttle, and Hampton[15] and merits consideration. By cutting across the first cartilaginous ring on either side of the proposed anastomosis in several places, the mucosa is allowed to flange out and be approximated face to face with mattress sutures. Neither granulations nor edema have been observed in their experiments. There is further experimental evidence[16] to indicate that wire is preferable to silk

as a suture material for tracheobronchial anastomoses, the incidence of granulations and strictures being distinctly less common with wire.

While it is undoubtedly a good principle to reinforce tracheobronchial anastomoses with viable tissue flaps, it proved not to be necessary in the case described above. Here, accurate approximation of edges was sufficient to prevent air leak, and the intramural blood flow was sufficient to provide for good healing despite extensive mobilization of the trachea above and below.

Summary

A case of stricture of the midthoracic trachea which occurred five weeks following presumed complete transverse fracture from nonpentrating injury, and which was successfully treated by excision of the stricture and end-to-end anastomosis of the trachea is presented. This represents the third case of intrathoracic tracheal stricture thus treated and the second such following trauma. Traumatic rupture of the trachea is far less common than rupture of the bronchus, but the two may be coincidental. Tracheal rupture in closed chest injuries may take the form of irregular longitudinal rents or complete transverse fractures. It is suggested that the former are more likely caused by sudden increased intratracheal pressure from a blow to the chest, while the latter are more likely due to direct compression of the trachea against the spine, though a combination of factors probably exists. The difficulties of treating secondary strictures emphasize again the necessity of early recognition and treatment of tracheobronchial rupture. A history of chest trauma plus hemoptysis, pneumothorax, or mediastinal or subcutaneous emphysema should suggest the diagnosis, which can then be confirmed by bronchoscopy. Some technical aspects of tracheobronchial anastomosis are discussed.

24 W. Gaston St.

REFERENCES

1. Kinsella, T. J., and Johnsrud, L. W.: Traumatic Rupture of the Bronchus, J. Thoracic Surg. 16:571, 1947.

2. Mahaffey, D. E.; Creech, O., Jr.; Boren, H. G., and DeBakey, M. E.: Traumatic Rupture of the Left-Main Bronchus Successfully Repaired 11 Years After Injury, J. Thoracic Surg. 32:312, 1956.

3. Rogers, W. L., in discussion on paper by Richards and Cohn.[7]

4. Laurier, R.; Messier, C. A., and Venne, J.: Traumatic Rupture of the Trachea, Union méd. Canada 84:278, 1955.

5. Thompson, J. V., and Eaton, E. R.: Intrathoracic Rupture of the Trachea and Major Bronchi Due to Crushing Injury, J. Thoracic Surg. 29:260, 1955.

6. Dark, J., and Jewsbury, P.: Fracture of the Trachea and Bronchus, Thorax 10:62, 1955.

7. Richards, V., and Cohn, R. B.: Rupture of the Thoracic Trachea and Major Bronchi Following Closed Injury to the Chest, Am. J. Surg. 90:253, 1955.

8. Bikfalvi, A., and Kassay, D.: Resection and Anastomosis of the Thoracic Portion of the Trachea for Cicatricial Stenosis, Internat. Abst. Surg. 102:555, 1956, in Surg. Gynec. & Obst., June, 1956.

9. Richards, V.: Personal communication to the author.

10. Kirkpatrick, E. R. G.: A Case of Traumatic Avulsion of a Main-Stem Bronchus from Its Lung, Treated by Immediate Pneumonectomy, Brit. J. Surg. 37:362, 1950.

11. Sale, T. A.: Fracture of the Bronchus, Brit. J. Surg. 41:625, 1954.

12. Shaw, R. R., in discussion on paper by Paulson and Shaw.[17]

13. Fox, R., in discussion on paper by Paulson and Shaw.[17]

14. Daughtry, D. C., in discussion on paper by Paulson and Shaw.[17]

15. Jackson, T. L.; Lefkin, P.; Tuttle, W. M., and Hampton, F.: An Experimental Study in Bronchial Anastomosis, J. Thoracic Surg. 18:630, 1949.

16. Pacheco, C. R.; Rivero, O., and Porter, J. K.: Experimental Reconstructive Surgery of the Trachea, J. Thoracic Surg. 27:554, 1954.

17. Paulson, D. L., and Shaw, R. R.: Bronchial Anastomosis and Bronchoplastic Procedures in Interest of Preservation of Lung Tissue, J. Thoracic Surg. 29:238, 1955.

Intra-Arterial Pressure Studies in Peripheral Arterial Reconstructions

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The approach to problems of arterial insufficiency in the lower extremity due to arteriosclerosis has shifted toward direct surgical attack on the involved vessels whenever possible. Case selection has largely been based on the demonstration of the pathologic anatomy by arteriography. Usually only cases showing a segmental occlusion have been felt suitable for arterial reconstructive procedures. Unfortunately, the highest failure rate in such reconstructions is in the commonest type of case, superficial femoral artery obstruction. Many of the cases which have resulted in dramatic angiographic and clinical success have come from the rather rare group of segmental distal aortic or iliac occlusions.

In an attempt to determine whether there were measurable changes in pressure relationships which might be called pathologic physiology accompanying the pathologic anatomy, the following study was carried out.

Method

Intra-arterial pressure recordings were made on five patients at the time of an arterial reconstructive procedure for segmental arteriosclerotic occlusion of the superficial femoral artery. These recordings were made by direct puncture of the vessel involved with a No. 20-gauge needle attached to a Sanborn electromanometer and a Twin-Viso recorder. Such pressure tracings were recorded from the proximal and distal channels before and after reconstruction if that operative procedure was successful. Tracings from normal subjects were obtained for comparative purposes. Femoral arterial pressures obtained by direct arterial puncture were also compared with brachial pressure obtained with the sphygmomanometer.

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Buswell Fellow in Surgical Research (Dr. Schenk).

Supported in part by a grant-in-aid from the Western New York Heart Association.

From the Department of Surgery, University of Buffalo School of Medicine and Edward J. Meyer Memorial Hospital.

Results

The common femoral artery pressure tracings from two normal subjects are shown in Figure 1, with the simultaneous brachial sphygmomanometer pressure determinations shown in parentheses. These data are correlated in Table 1, which shows the direct femoral measurements falling below the brachial values in each instance, with rather small discrepancies in the systolic readings (3 and 5 mm., respectively) but wider separation in the diastolic readings (10 and 17 mm., respectively).

CASE 1.—*Superficial femoral thromboendarterectomy.*

The pressure tracings recorded proximal and distal to the obstructed segment are seen in Figure 2 before and after the operative procedure. The data from this case are presented in Table 2. Three points seem worthy of comment here. First, the systolic pressure in the proximal femoral artery is 25 mm. Hg lower than the systolic pressure in the brachial artery, and the pulse pressure in the femoral artery is reduced. Second, the pressure in the femoral artery distal to the block is reduced to almost half the pressure just proximal to the occlusion and is nonpulsatile. Third, a significant increase in systolic pressure occurs in the distal segment after reconstruction, in spite of a fall in the diastolic pressure in the proximal segment, and the pressure in the distal segment is now pulsatile.

CASE 2.—*Superficial femoral artery by-pass homograft.*

Recordings from this patient are seen in Figure 3 and the data tabulated in Table 3. Again, it will be noted that the systolic pressure in the proximal femoral segment is much lower

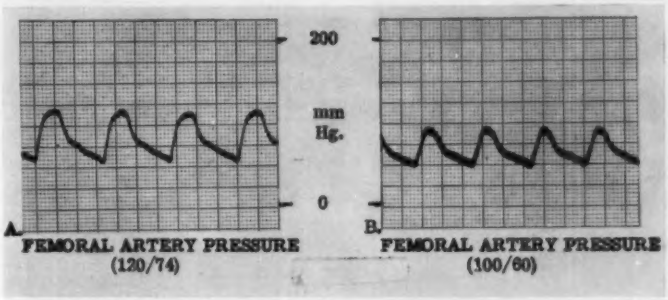

Fig. 1.—Femoral artery pressure recordings from two normal patients. Figures in parentheses are simultaneous pressures.

(50 mm. Hg) than the simultaneous brachial systolic pressure. Pulse pressure and mean pressure in the distal femoral segment are low. After the reconstructive procedure the systolic pressure in the distal femoral segment has been increased 20 mm. Hg in spite of a fall of 30 mm. Hg in the systolic pressure of the proximal femoral segment.

TABLE 1.—*Comparison of Sphygmomanometer Brachial Pressure with Direct Intra-Arterial Recording of Femoral Pressure in Two Normal Subjects*

Brachial Pressure (Sphygmomanometer)	Femoral Pressure (Direct Intra-Arterial)	Difference
120/74	117/57	—3/—17
100/60	95/50	—5/—10

CASE 3.—*Superficial femoral artery by-pass homograft.*

The pressure recordings from this patient are seen in Figure 4 and the data assembled in Table 4. This case differs from the first two presented in that the proximal femoral pressure exceeds the brachial pressure both before and after the reconstruction. The marked improvement in distal pulse pressure is immediately evident from inspection of the tracings. The reconstruction resulted in

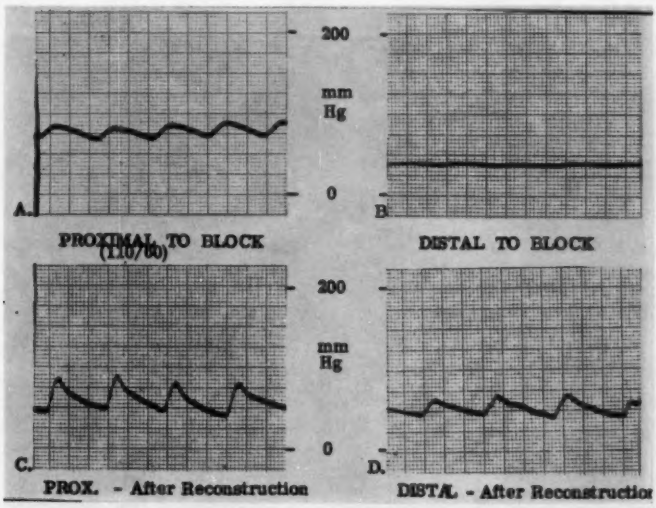

Fig. 2.—Femoral artery pressure recordings before and after thromboendarterectomy. Figures in parentheses are simultaneous brachial pressures.

TABLE 2 (Case 1).—*Arterial Pressure Values* Before and After Superficial Femoral Thromboendarterectomy*

	Brachial	Proximal Femoral	Difference	Distal Femoral	Change in Distal Femoral Pressure After Reconstruction
Prior to reconstruction	110/60	85/70	—25/+10	40/40	
After reconstruction	--	85/50	--	70/45	+30/+5

* Brachial pressure obtained with sphygmomanometer. Femoral pressure is direct intra-arterial measurement.

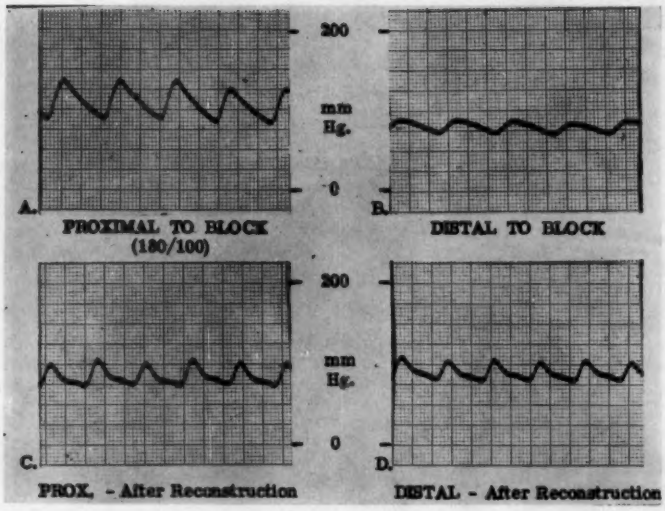

Fig. 3.—Femoral artery pressure recordings before and after by-pass homograft. Figures in parentheses are simultaneous brachial pressures.

TABLE 3 (Case 2).—*Arterial Pressure Values Before and After Superficial Femoral Artery By-Pass Homograft*

	Brachial	Proximal Femoral	Difference	Distal Femoral	Change in Distal Femoral After Reconstruction
Prior to reconstruction	180/100	130/85	—50/—15	85/70	
After reconstruction	150/90	100/75	—50/—15	105/80	+20/+10

Fig. 4.—Femoral artery pressure recordings before and after by-pass homograft. Figures in parentheses are simultaneous brachial pressures.

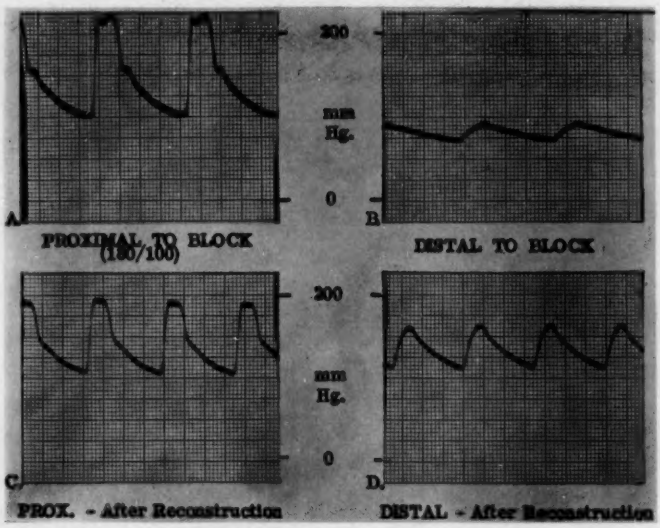

TABLE 4 (Case 3).—*Arterial Pressure Values Before and After Superficial Femoral Artery By-Pass Homograft*

	Brachial	Proximal Femoral	Difference	Distal Femoral	Change in Distal Femoral After Reconstruction
Prior to reconstruction	180/100	215/100	+35/0	90/75	
After reconstruction	180/100	190/105	+10/+5	160/110	+70/+35

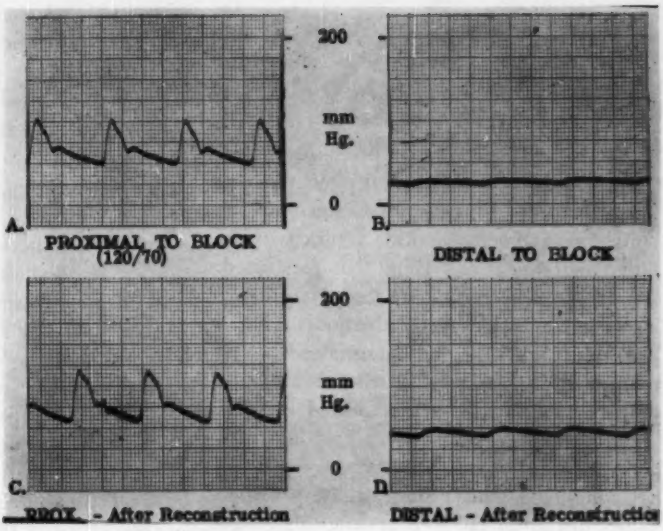

Fig. 5.—Femoral artery pressure recordings before and after crimped-nylon by-pass reconstruction. Figures in parentheses are simultaneous brachial pressures.

TABLE 5 (Case 4).—*Arterial Pressure Values Before and After Superficial Femoral Artery Crimped-Nylon By-Pass*

	Brachial	Proximal Femoral	Difference	Distal Femoral	Change in Distal Femoral After Reconstruction
Prior to reconstruction	120/70	100/50	—20/—20	25/25	
After reconstruction	125/70	115/55	—10/—15	50/40	+25/+15

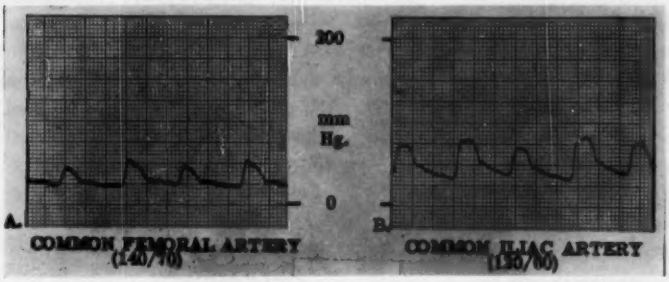

Fig. 6.—Arterial pressure recordings prior to anticipated reconstruction in arteriosclerotic occlusive disease. Figures in parentheses are simultaneous brachial pressures.

an increase of 70 mm. Hg in the distal femoral systolic pressure in spite of a fall of 15 mm. Hg in the proximal femoral pressure during the procedure.

CASE 4.—*Superficial femoral artery crimped nylon by-pass.*

This patient's studies are shown in Figure 5 and Table 5. Worthy of note here is the rather slight change in distal pressure after reconstruction in spite of adequate proximal pressure. This prosthesis occluded on the fifth postoperative day.

CASE 5.—*Exploration of superficial femoral artery.*

The data from this case are assembled in Figure 6 and Table 6. It can be noted that the systolic pressure in the proximal femoral artery is 90 mm. Hg below that recorded in the brachial artery. It was felt that the proximal arterial pressure (50/25) was inadequate to maintain patency in any type of reconstruction; therefore, the operative plan was changed and a lumbar sympathectomy performed. During the latter procedure a direct pressure tracing was obtained from

TABLE 6 (Case 5).—*Arterial Pressure Values Recorded at Exploration of Superficial Femoral Arterial Obstruction*

	Brachial	Proximal Artery	Difference
Common femoral	140/70	50/25	—90/—45
Common Iliac	120/60	75/35	—45/—25

the common iliac artery, as seen in Figure 6*B*. Here, again, the pressure was much lower than the simultaneously recorded brachial pressure.

Comment

In the data presented, pressures determined by direct intra-arterial puncture have been compared with those obtained by the sphygmomanometer, and the accuracy of the latter determinations could be questioned. In an excellent review of the problems of sphygmomanometer determination of blood pressure, Bordley and associates [1] summarize with the statement that a mean error of ±8 mm. Hg may be expected in individual readings of systolic and diastolic pressures. Allowing for such a range of error in the method, most of the pressure values discussed fall well outside this range of theoretical error.

Although this study is not a statistical one and the possibility exists that single observations may be misleading, it seems that certain statements may be justified. The discrepancy which may exist between the sphygmomanometer brachial pressure determination in the arm and the direct arterial pressure measurement in the femoral vessel is most easily interpreted as being the result of significant obstruction existing proximal to that femoral vessel which has not been recognized clinically or by arteriogram. Grossly inadequate proximal pressure may be the cause of some otherwise unexplained reconstructive failures. A proximal channel which is anatomically adequate as shown by angiography may be quite inadequate functionally.

When adequate proximal arterial pressure is present, a homograft reconstruction results in a significant improvement in pulse pressure distal to the occlusion. In a single case in which a prosthetic reconstruction was carried out, very little improvement in distal pulse pressure resulted in spite of adequate proximal pressure. This interference with pulse transmission by prosthetic materials has been confirmed by experimental work.[2] Whether pulse pressure has important physiological significance has not yet been determined, and the evidence on this point is conflicting.[3]

Summary and Conclusions

In normal persons in the supine position the femoral intra-arterial pressure as determined by direct measurement correlates closely with the brachial pressure as determined with the sphygmomanometer.

In a patient with segmental occlusive disease in the superficial femoral artery the pressure in the vessel proximal to the obstruction may be significantly lower than the brachial pressure recorded simultaneously.

This pressure differential may be due to an unrecognized proximal obstruction, in spite of demonstration of adequate channels by arteriography.

Inadequate proximal pressure may be the cause of failure in some vascular reconstructions.

Successful arterial homograft reconstruction produces significant increase in the pulse pressure in the distal arterial channel.

Femoral artery reconstruction with a crimped nylon prosthesis resulted in marked damping of the pulse pressure in the distal channel in spite of adequate proximal pressure.

462 Grider St. (15).

REFERENCES

1. Bordley, J., III; Connor, C. A. R.; Hamilton, W. F.; Kerr, W. J., and Wiggers, C. J.: Recommendations for Human Blood Pressure Determinations by Sphygmomanometers, Circulation 4:503, 1951.

2. Schenk, W. G., Jr.; Cosgriff, J. H., Jr., and Gray, J. G.: Hemodynamic Changes Resulting from Blood Vessel Grafts and Prostheses, Surg. Gynec. & Obst. 103:213, 1956.

3. Wesolowski, S. A., and Welch, C. S.: Experimental Maintenance of the Circulation by Mechanical Pumps, Surgery 31:769, 1952.

Clinical Aspects and Management of Sacrococcygeal Teratoma

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Although sacrococcygeal teratoma cannot be considered a rare tumor, it is sufficiently uncommon that most physicians do not acquire personal experience with this entity. From the calculations of Calhet and Fochier, congenital tumors of the sacrococcygeal region occur once in 34,582 births.[3] Teratomas represent only a small percentage of these tumors. To date there are approximately 450 cases described in the literature.

Sacrococcygeal teratomas are recognized at birth in about 90% of the cases. The remainder are seen in older children and, rarely, in adults. At least 75% of the cases have occurred in females. A large percentage of infants with sacrococcygeal teratoma are born dead or die shortly after birth.[4]

Three cases are presented which highlight the problems of diagnosis and management of these tumors.

Report of Cases

CASE 1.—A full-term girl was born at the 5005th U. S. A. F. Hospital on Feb. 18, 1954, weighing 8 lb. 12¼ oz. (3983 gm.). Delivery of the infant's pelvis was delayed because of impaction in the birth canal by a large tumor mass in the sacrococcygeal region. The infant cried immediately, and physical examination revealed a large cystic mass in the sacrococcygeal area, measuring approximately 5.5×8.5×8.5 cm. (Fig. 1). The anus appeared to be displaced anteriorly by the mass. The skin overlying the tumor was congested and bluish-purple in color. X-rays of the lumbosacral region revealed a soft-tissue mass overlying the sacrococcygeal area, which contained irregular patches of increased densities, suggesting the presence of calcification (Fig. 2). The diagnosis of sacrococcygeal teratoma was made, and operation was performed eight hours after birth.

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From the Surgical Division, the Montefiore Hospital.

With the infant under endotracheal general anesthesia, an inverted V-incision was made above the tumor mass through normal-appearing skin (by one of us, B. S.). The tumor was adherent to the coccyx, which was excised, and the mass was readily dissected from the rectum and the surrounding structures. The levator ani muscles around the rectum were approximated to the presacral fascia, and the wound was closed in layers. The wound healed per primum, and the child was discharged on the eighth postoperative day.

Pathologic Examination.—Gross: The specimen was an ovoid tumor mass, weighing 187 gm. (Fig. 3). The surface of the tumor was lobular, due to numerous cystic areas, and was surrounded by an intact capsule. The cut surface of the specimen appeared cellular and edematous.

Microscopic: The sections showed marked variation of architectural pattern throughout. Numerous cysts were present, lined by glandular epithelium, which varied from cuboidal to columnar in type. Some of the areas were composed of squamous epithelium, respiratory epithelium, smooth muscle, and cartilaginous material. The cellular architecture throughout was quite uniform.

Subsequent Course.—Examination of the child six months postoperatively revealed normal growth and development and no recurrent disease (Fig. 4).

Diagnosis.—Sacrococcygeal teratoma, benign.

Comment.—In this case, the large sacrococcygeal teratoma produced dystocia, as well as ischemia and impending necrosis of the overlying skin. By uneventful surgical excision eight hours after birth, the danger of secondary infection following skin necrosis and potential malignant degeneration was avoided.

CASE 2.—A five-year-old girl was admitted to Montefiore Hospital on June 1, 1953, because of a recurrent sacrococcygeal tumor. On examination shortly after birth, a cystic mass about the size of a walnut had been noted at the lower end of the spine (Fig. 5*A*). X-rays of the pelvis and sacrococcygeal regions showed a mass with calcification. On Oct. 27, 1947, at 3½ months of age, the child had been operated upon at another institution. Three cystic masses were found, two of

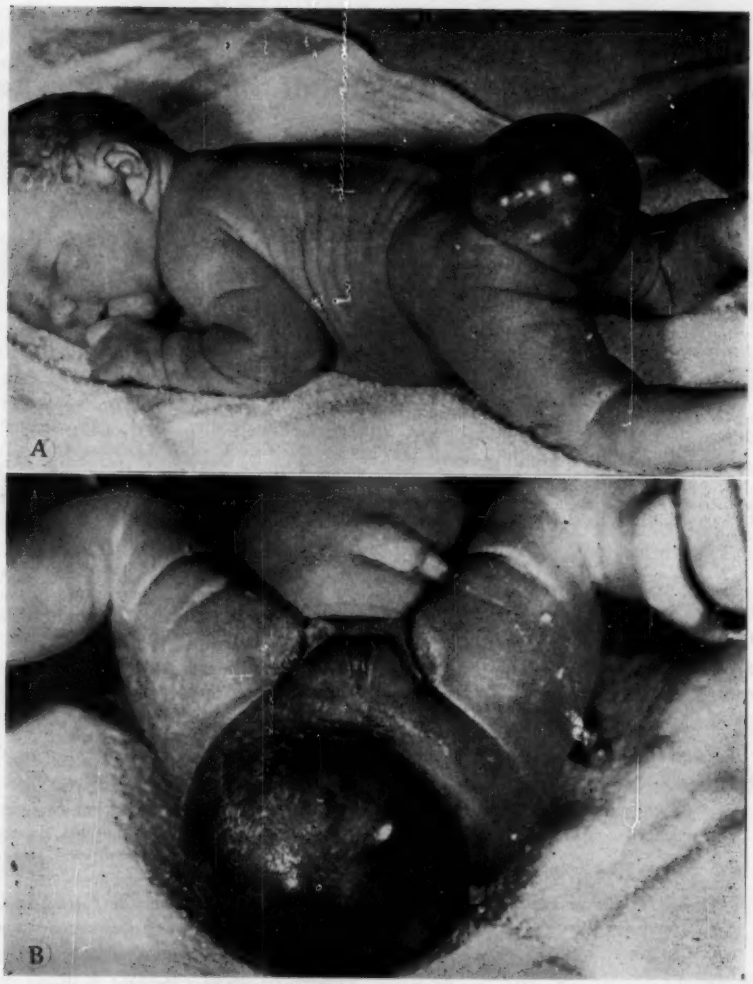


Fig. 1 (Case 1).—Photographs of a newborn infant with a large sacrococcygeal teratoma that (*A*) caused dystocia by impaction of the infant's pelvis in the birth canal and (*B*) displaced the anus anteriorly. The skin overlying the mass was congested and bluish-purple in color.

which were removed; but during the dissection of the second mass the cyst was entered. By this time the patient's condition apparently became poor, and the operation was curtailed. The residual third cyst was unroofed, packed with gauze, and drained. The wound healed within three weeks.

Pathologic Examination.—Gross Appearance: The specimen consisted of two thick-walled cysts, the larger of which measured 2.5 cm. in diameter.

Microscopic Study: Sections of the larger cyst revealed it to be part of a mixed tumor. The inner surface was lined with a mucosa which, for the most part, was colonic in type. It included a muscularis muscosa, a submucosa, and a well-developed, thick muscular coat. Over part of the surface, however, the character of the mucosa resembled that of the duodenum, and there also was a small island of rudimentary pancreatic tissue. The second cyst showed an irregular cavity lined with a pseudostratified columnar epithelium, which in places was ciliated.

Diagnosis.—Cystic teratoma.

Course.—In November, 1949, two years after the original operation, a cystic mass was again reported as palpable in the sacrococcygeal region, but reoperation was not advised at that time. When first seen by us, in 1953, the sacrococcygeal mass was still present but apparently had not increased

Fig. 2. (Case 1).—Roentgenogram of the lumbosacral region, showing the soft-tissue mass with irregular patches of calcification.

in size appreciably (Fig. 5*B*). On rectal examination two cystic masses could be felt partially encircling the rectum on either side. Reoperation for complete removal of the residual tumor was performed on June 5, 1953. The previous scar was excised, and the dissection was carried laterally on both sides of the cystic mass (E. S. H.). A tube previously placed in the rectum was an aid in identifying this structure and in safeguarding it from injury during the dissection. The teratoma peeled away from the rectum easily and was completely excised in continuity with the coccyx. The levator ani muscles were sutured to the presacral fascia, and the skin was closed with silk sutures. The postoperative course was uneventful, and the patient was discharged on June 13. Follow-up visits to the present reveal normal growth and development, with no evidence of recurrent disease in the sacrococcygeal area. Rectal examination is entirely negative.

Pathologic Examination.—Gross Findings: The specimen consisted of an irregular ovoid mass of tissue with a multinodular surface, measuring 11×8×5 cm. (Fig. 6). The mass resembled adipose tissue, with a cystic space containing a few hairs and dark-green viscid fluid.

Microscopic Findings: Multiple sections throughout the mass revealed an irregular arrangement of tissue derived from all three germ layers. In large sheets of mature adipose tissue were irregular masses of dense collagen bundles. These contained aggregates of squamous epithelial cells, foci of glial tissue cells, and cystic spaces lined by squamous, pseudostratified columnar ciliated, and columnar epithelium. Striated muscle fibers were also present. In some of the cysts hair shafts were noted.

Diagnosis.—Sacrococcygeal teratoma, benign.

Comment.—This 5-year-old girl had a sacral tumor which had been inadequately managed in infancy. Blood replacement during the resection was insufficient, resulting in shock and rapid termination of the procedure by opening the cyst and cutting across the tumor. When an obvious recurrence of the teratoma developed two years later, complete excision was indicated promptly because of the malignant potential of these tumors. Fortunately, malignant change had not occurred before the second, and definitive, operation was performed, at the age of 5 years.

Case 3.—An 8-day-old full-term male infant, born by normal spontaneous delivery, and weighing 6 lb. 3 oz. (2806 gm.), was admitted to the Mount Sinai Hospital, New York, on Dec. 30, 1947. Physical examination was essentially unremarkable except for a mass in the sacral area, which projected posteriorly from beneath the coccyx and pushed the anus forward. The mass measured 3×2×2 in. (7.5×5×5 cm.) and was lobulated and cystic. It was easily palpable posteriorly on rectal examination. At operation, on Jan. 7, 1948 (E. S. H.), a horizontal curvilinear incision was made over the apex of the mass, and the encapsulated tumor was dissected from the retrorectal space. The tumor was removed in continuity with the coccyx and a wedge of sacrum, because of invasion into the sacrum. The child made a good recovery and was discharged on the 37th hospital day.

Pathologic Examination.—Gross: The specimen was a globular mass, measuring 7×5.5×4 cm. At one point the capsule was incomplete, and pinkish-gray soft tissue was seen. On cross section the tumor was seen to be roughly divided into two portions. One area contained soft, gray-pink, and apparently cellular tissue. The other portion had numerous cysts containing mucoid material.

Microscopic: The tumor contained all three components of a teratoma. It was predominantly glandular but contained also cartilaginous, neural, smooth muscle, and loose fibrous connective tissue. The glands were of bizarre shapes and sizes. Many of them were lined by columnar epithelium

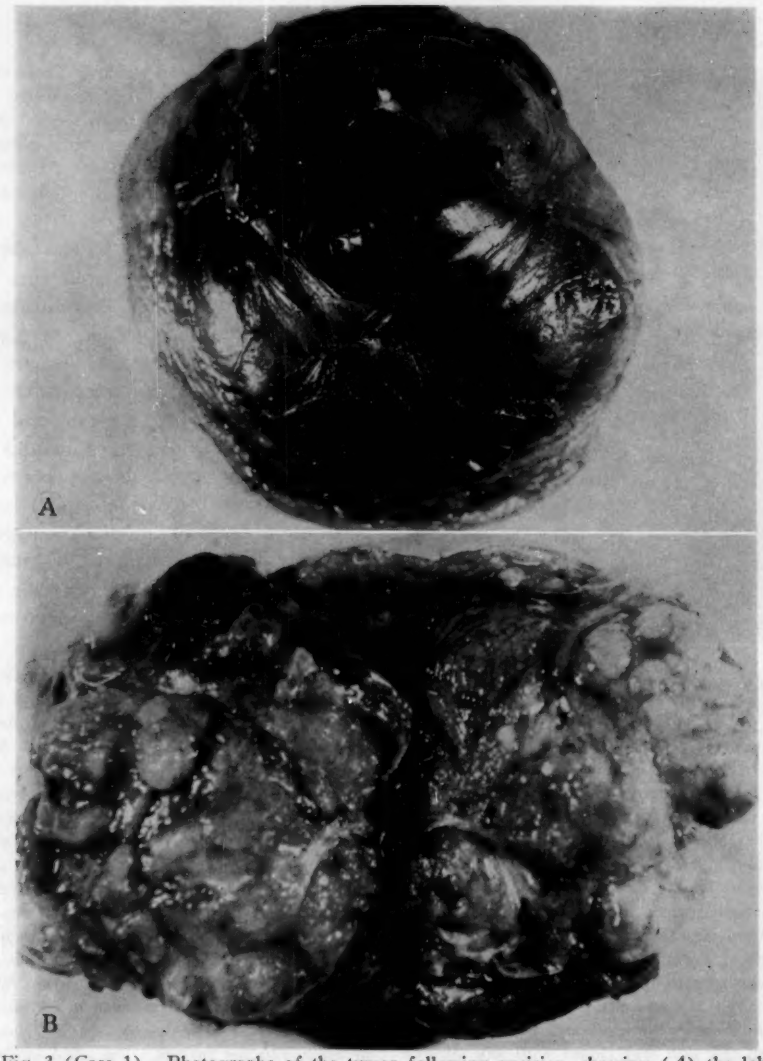


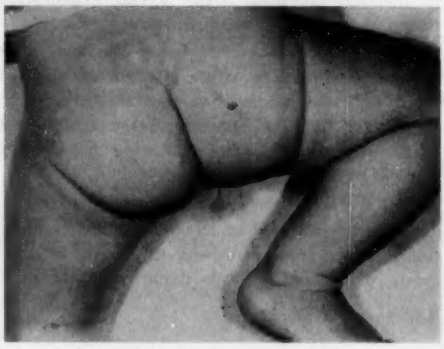
Fig. 3 (Case 1).—Photographs of the tumor following excision, showing (*A*) the lobular cystic surface surrounded by an intact capsule and (*B*) the cut surface, which appeared cellular and edematous.

similar to that of the gastrointestinal tract. Stratified squamous epithelium was present, as well as apocrine glands with large clear cells. In some glands the lining epithelium was disrupted and replaced by a sheet of varying-sized polygonal cells. These cells contained a scant amount of pale eosinophilic cytoplasm and moderately large, irregular, ovoid vesicular nuclei with nucleoli and atypical mitotic figures.

Diagnosis.—Malignant teratoma, containing adenocarcinoma.

Subsequent Course.—The child's second admission to the Mount Sinai Hospital was on April 20, 1948, because of inability to extend his right leg during the previous four days. X-rays revealed an area of diffuse bone destruction in the

Fig. 4 (Case 1).—Photograph taken six months postoperatively, showing normal growth and development and no recurrent disease.



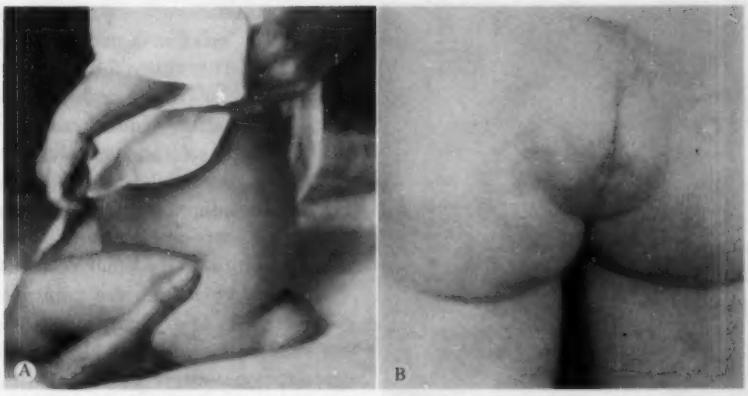


Fig. 5 (Case 2).—Photographs demonstrating (*A*) the sacrococcygeal mass at 3 months of age and (*B*) the recurrent mass at 6 years of age.

distal half of the femur, and a linear fracture extended through the infiltrated area (Fig. 7). The diagnosis of malignant teratoma metastatic to bone with pathologic fracture was confirmed by open biopsy. Radiotherapy was administered to the femur, with some improvement. The third admission was on Feb. 23, 1949, in terminal condition. Examination showed distant breath sounds in both lower lobes, with numerous rales and rhonchi, and there was an abdominal mass filling both lower quadrants. The patient died 12 hours after admission.

Autopsy.—Autopsy findings were malignant sacrococcygeal teratoma with metastases to retroperitoneal nodes, lungs, diaphragm, right femur, right hip joint capsule, spinal cord, and lumbar vertebrae. There were compression of both ureters by retroperitoneal lymph node metastases, with bilateral hydronephritis and hydroureter, and atelectasis of the lower lobes of both lungs, with bronchopneumonia.

Comment.—This case is a classic example of the tragic chain of events seen in cases of malignant sacrococcygeal teratoma with metastases which commonly occur in the bones, liver, lungs, and lymph nodes.

Fig. 6 (Case 2).—Photographs of the resected recurrent tumor, showing (*A*) the multinodular surface and (*B*) the solid and cystic components on cut section.

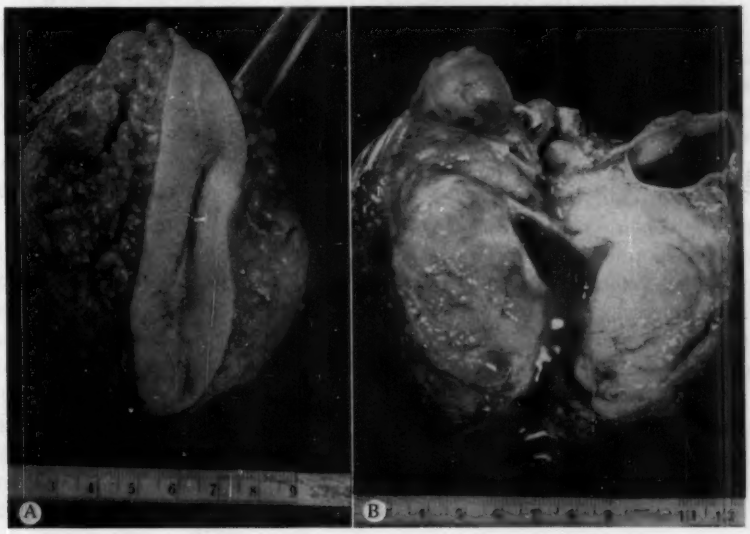


Fig. 7 (Case 3).—A roentgenogram of a 4-month-old boy with a malignant sacrococcygeal teratoma, demonstrating metastasis to the distal half of the femur with pathologic fracture.

Comment

Sacrococcygeal teratomas are usually obvious at birth. They present as a mass protruding between the rectum and the sacrum and may displace the anus anteriorly and to the side. The tumor may vary in size from an insignificant 2 cm. nodule to a large, bulky mass, causing difficulty in the delivery of the trunk of the infant, as in Case 1.[8,12] Infrequently the occult variety is encountered in which the presacral tumor does not project onto the surface of the body, and the condition may not be recognized until its continued growth causes obstruction of the rectum, urethra, or the ureters by compression.[2,5,13] Rapid growth of the tumor is not unusual, since it parallels that of the child. The directions of growth may be posteroinferiorly into the buttocks, anteriorly into the pelvis, displacing and surrounding the pelvic organs, and upward retroperitoneally presenting as a large abdominal mass.[1,13]

On examination the tumor may present as a cystic or solid mass or any combination of the two. It is covered by skin, which may be normal, or tense and ulcerated. The x-ray frequently demonstrates amorphous and scattered calcium deposits in the soft-tissue mass or well-formed bone or teeth. Digital examination of the rectum is essential to determine the extent of the tumor and its relation to the other pelvic structures. These tumors often are dumbbell- or hourglass-shaped, and Renner and Goodsitt [11] reported a case with a double tumor. Rectal examination will reveal such presacral extensions or second tumors.

A mass in the sacral region may be caused by a diversity of lesions, which must be differentiated in order to institute the proper therapy. Among the frequently listed causes of a swelling in this area are meningocele, dermoid cyst, neurogenic tumors, chordoma, teratoma, pilonidal cyst, abscess, and benign tumors of the buttocks. A careful physical examination and x-ray studies usually lead to a correct diagnosis.

Sacrococcygeal teratomas contain tissue representing each of the three germinal layers. On gross section they usually have both cystic and solid elements. In some instances segments of intestine, brain, teeth, skin, hair, and bone may be grossly recognizable. Microscopically, there is a marked variation in architectural pattern, representing a helter-skelter intermingling of the various tissue elements. Skin, intestinal mucosa, respiratory mucosa, nerve tissue, cartilage, bone, fat, striated muscle, and salivary and pancreatic glands are those most commonly seen.[5,10]

Most of the complications attributed to this tumor are due to pressure, infection, or malignancy. A large tumor mass extending into the pelvis may cause obstruction of the lower portion of the intestinal or urinary tract by compression. Necrosis of the tumor or the overlying skin may produce infection of sufficient severity to be fatal.[10] The greatest threat to life is due to the malignant potential of the sacrococcygeal teratoma. The

incidence of malignancy rises as more series of cases are being reported. By 1939, it was found that 9% of the reported cases were malignant.[8] A review by Ravitch and Smith listed the incidence at 17%,[10] and 20% was found by Hickey and Layton.[7] Pathologically, the type of malignancy is usually a papillary adenocarcinoma, but embryonal carcinoma and malignant neural tissue have also occurred. They invade adjacent structures and metastasize commonly to the liver, lungs, bones, and lymph nodes.

There are no clinical criteria whereby one can predict accurately the malignant potential of these tumors. Calcification may be present in both benign and malignant lesions. However, if on clinical examination of the patient, the tumor presents evidence of adult tissue, such as muscle twitchings and intestine with peristalsis, it is usually benign.[6]

Definitive total excision of the tumor, as soon as the diagnosis is made and the child's condition warrants, is the accepted therapy for sacrococcygeal teratoma. Prematurity or the neonatal period is not a contraindication to surgery. Hickey and Layton, in their analysis of the reported cases, conclude that there is an increased incidence of cancer with delayed therapy, and malignant transformation occurs most frequently between the ages of 4 months and 5 years.[7]

The essential features of the surgical therapy are clearly outlined by Gross, Clatworthy, and Meeker.[5] A vein is cannulated in all cases so that blood can be given during surgery. The posterior approach, described by Pearse,[9] with the child in face-down position and the abdomen and pelvis raised over a sandbag or folded sheet, is used. A large tube or petrolatum U. S. P. (Vaseline) gauze packing is inserted in the rectum to facilitate its identification and avoid injury during the dissection. An elliptical incision is made and the tumor completely dissected from the surrounding structures. Total excision of the coccyx in continuity with the tumor is an important step in the prevention of recurrence. Meticulous hemostasis is effected, and the rectum and perineal structures are restored to a more normal position by suturing the perianal portion of the levator ani muscles to the presacral fascia during the layer closure of the wound. The child is kept in a face-down position during the first postoperative week to avoid contamination of the operative site by urine or feces.

Recurrent tumor, as in Case 2, does not necessarily mean that malignant change has occurred. If no metastases are discovered, early secondary attempts at complete excision are indicated, utilizing the same approach and principles as described.

Summary

Sacrococcygeal teratoma is seen most commonly in infants and is usually recognized at birth in 90% of the cases.

The complications attributed to the tumor are due to pressure, infection, or malignancy.

Definitive total excision of the tumor and the coccyx, as soon as the diagnosis is made and the child's condition warrants, is the accepted therapy.

Recurrent tumor should be treated by prompt secondary excision provided no metastases are discovered.

Three cases are reported which clearly demonstrate the clinical aspects and the management of sacrococcygeal teratoma.

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REFERENCES

1. Arnheim, E.: Retroperitoneal Teratoid Tumors in Infancy and Childhood, J. Mt. Sinai Hosp. 10:355, 1943.

2. Brown, R. K., and Brown, E. C.: Sacrococcygeal Teratoma with Urinary Retention, Arch. Surg. 60:535, 1950.

3. Chaffin, L.: Clinical Aspects of Sacrococcygeal Teratomas, Surg. Gynec. & Obst. 69:337, 1939.

4. Ewing, J.: Neoplastic Diseases: A Treatise on Tumors, Ed. 4, Philadelphia, W. B. Saunders Company, 1940.

5. Gross, R. E.; Clatworthy, H. W., Jr., and Meeker, I. A., Jr.: Sacrococcygeal Teratomas in Infants and Children: A Report of 40 Cases, Surg. Gynec. & Obst. 92:341, 1951.

6. Hansmann, G. H., and Berne, C. J.: Sacrococcygeal Teratomas, Arch. Surg. 25:1090, 1932.

7. Hickey, R. C., and Layton, J. M.: Sacrococcygeal Teratoma: Emphasis on the Biological History and Early Therapy, Cancer 7:1031, 1954.

8. Kurzrock, J., and Pleshette, N.: Dystocia Due to Fetal Teratoma, Am. J. Obst. & Gynec. 35:326, 1938.

9. Pearse, H. E.: Removal of Ventral Tumors of the Sacrum by the Posterior Route, Surg. Gynec. & Obst. 33:164, 1921.

10. Ravitch, M. M., and Smith, E. I.: Sacrococcygeal Teratoma in Infants and Children, Surgery 30:733, 1951.

11. Renner, R. R., and Goodsitt, E.: Sacrococcygeal Teratoma: Report of a Case of Double Tumor in a Newborn Infant, Am. J. Cancer 24: 617, 1935.

12. Walls, J. J.: Obstructed Labour Due to Sacral Tumor of Foetus, Brit. M. J. 1:487, 1946.

13. Woodruff, S., and Begner, J. A.: Sacrococcygeal Teratoma in an Infant of 5 Months Causing Acute Urinary Obstruction, J. Urol. 54: 177, 1945.

An Anesthetic Technique for Cardiac Surgery Which Utilizes 100% Oxygen as the Only Inhalant

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The purpose of this paper is to present an anesthetic technique for cardiac surgery in which no inhalation agent is used other than 100% oxygen.

It should be pointed out that the evolution of the method entailed no predetermined ideas about producing an analgesic state in the absence of an anesthetic inhalant this property, but, rather, was the outcome of clinical observations on various patients during cardiac surgery dating back to the latter part of 1952.[1] It is believed that this technique accomplishes an analgesic state similar to that which has been attributed to ether and oxygen, but avoids the necessity of giving ether.[2]

The Preoperative Visit

The anesthesiologist's visit to the patient the evening before surgery is an important part of the procedure, since at that time he must always do a thorough chest examination whether or not the patient has had such an examination prior to this time. Recent chest films do not form the basis for omitting this procedure. It is quite possible that a pleural effusion of sufficient magnitude may be present to interfere seriously with expansion of the lung during surgery.

The Technique

One hour before surgery the patient is given a subcutaneous injection of 100 mg. of meperidine hydrochloride (Demerol) in addition to 0.4 mg. of scopolamine hydrobromide. The reason for the preference for meperidine is the slight drowsiness it produces. Scopolamine, rather than atropine, is chosen because of the amnesic property it possesses.

The technique of anesthetizing the patient is begun by slowly injecting intravenously 2.5% thiopental sodium (thiopentone) until an effective dose has been given, the effect being the stage at which the patient goes to sleep. (An average amount would be about 375 mg.). A rapid rate of injection serves no useful purpose; indeed, by injecting the drug rapidly, it is not possible to determine an effective dose, since one must allow for the time lag between the time of injection and the effect of the drug. It has been our experience that a rapid injection can result in a precipitous fall in blood pressure.

While the injection of thiopental is going on, it is extremely important to have the patient breathe 100% oxygen by mask. The treatment for hypoventilation as a result of respiratory-center depression is manually assisted respiration. At no time during this procedure is the patient allowed to hypoventilate. Should oxygen delivered in this manner be omitted, it is possible occasionally to observe the presence of an ST depression in the electrocardiogram, which is corrected by adequate ventilation.

Having arrived at an effective dose of thiopental sodium, 4 mg. of decamethonium bromide is given intravenously. From this stage the patient's respirations are controlled manually for the duration of the operation. Under direct vision, 2.0 cc. of 10% cocaine is atomized into the trachea in order to

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reduce or prevent the stimulus of endotracheal intubation. Controlled respiration is maintained for an additional three or four minutes before the intubation is performed.

About 15 minutes is taken to position, prepare, and drape the patient. At this time 25 mg. of meperidine hydrochloride is given intravenously, i. e., just prior to commencement of the operation.

It is not necessary to give to these patients an intravenous injection of tubocurarine chloride for relaxation, since relaxation to that extent is not required for cardiac surgery. Nor is it necessary to produce paralysis in order to immobilize the patient while the skin is being incised. However, according to our own feelings on the subject, if during the procedure of controlled respiration there is felt an increasing resistance to the intermittent positive pressure that is being used, we do not hesitate to inject 9 mg. of tubocurarine chloride in order to relax the intercostal muscles. No additional injection of this drug is required.

That the patient is in a light plane of anesthesia may be confirmed by the fact that one may observe that the patient is able to respond to simple commands, such as "Open your eyes," or to nod the head in response to "Do you hear me?" Needless to say, this is rather a curious and unlooked-for state; it is not sought after, but does occur. If for any reason the anesthesiologist ceases to control the respirations, even if only for a short time, it can be predicted that the patient will have a tendency to waken.

Removal of the retractors in preparation for closing the thorax usually results in the patient showing signs of movement. In order to prevent this response, it is usually, though not invariably, necessary to use something more than oxygen alone for closure. Satisfactory results may be obtained by using 4 liters of oxygen with 4 liters of nitrous oxide.

So far, we have been describing the aspect of the anesthetic technique used in cardiac surgery. It is our feeling that one cannot separate the anesthetic method from the surgical procedure, since the success of one depends upon the other. A mutual understanding between the surgeon and the anesthesiologist concerning the problems that present themselves during cardiac surgery is a fundamental concept, so necessary for consistently good results. Gentleness in handling tissues is a necessity for the success of this form of anesthesia. Retraction against bronchi or excessive manipulation of the lung is poorly tolerated. One can, however, manipulate the pericardium or operate upon the heart or great vessels without producing pain stimuli which break through this analgesic state. The myocardium remains pink and is relatively less likely to develop abnormal rhythms than when inhalant anesthetic agents are used.

Comment

Since September, 1953, we have used this technique for cardiac surgery. The outstanding feature of this method is the remarkable cardiac stability in the presence of the stimulating effect of surgery. Among the patients have been approximately 200 mitral valvulotomies and approximately 150 other cardiac procedures. Most of the operations have lasted from 90 to 180 minutes.

It is our belief that adequate ventilation by means of manually controlled respirations using a high oxygen content, plus the elimination of carbon dioxide, is the most important feature contributing to cardiac stability.

While it has been shown by Haldane and Priestley[3] that three minutes of voluntary hyperventilation can reduce arterial pCO_2 from 40 to about 14 mm. Hg, the mixed venous pCO_2 is reduced only from 46 to about 34 mm. Hg.

In clinical anesthesia Rollason and Parkes[4] deliberately subjected a carefully controlled series of patients to hyperventilation of 20 liters per minute for one to one and one-half hours without serious alterations of the acid-base balance.

Hyperventilation of a greater degree and of a longer duration was noted by Crane et al.[5] in poliomyelitis patients in tank

respirators. These patients demanded ventilation sufficient to reduce and maintain alveolar pCO_2 at an average of 25 mm. Hg for as long as they were in the tank—some of them as long as five months, and without evidence of ill-effect.

Since 100% oxygen is used in this technique, the question of oxygen toxicity may occur to some. The physiology of high tissue oxygen tension is not well known, but its effect on the lung and brain has been investigated. Penrod [6] has shown that the pathologic process of oxygen "damage" to the lung is one of massive atelectasis and that this is reversible by positive-pressure inflation or intermittent exposure to air.[7] This was demonstrated in guinea pigs at 4 atmospheres and in cats at 6 atmospheres.[8]

Ordinarily, symptoms of oxygen toxicity (dyspnea, nausea, twitching, visual disturbance, convulsions), are not observed at one atmosphere pO_2. However, under conditions of heavy exercise or shallow respirations for prolonged periods of time, symptoms have been reported on breathing oxygen at one atmosphere.[9] The authors could find not a single case of oxygen toxicity in resting man at one atmosphere. It has been shown by Lambertsen et al.[10] that brain tissue oxygen tension must rise before symptoms of oxygen toxicity will occur. Ordinarily, high oxygen pressure indirectly produces a cerebral vasoconstriction, which prevents exposure of the brain to high oxygen tensions. Among factors which make the brain more susceptible to oxygen toxicity is exercise (high cardiac output) or high arterial CO_2 (hypoventilation) or both, the mechanism being one of cerebral vasodilatation. It is interesting to note that hyperventilation exerts a protective effect and will abort symptoms of oxygen toxicity at 3½ atmospheres. The slight increase in jugular carbon dioxide content with oxygen at one atmosphere is considered insignificant.

The accompanying Table shows the results of blood gas analyses of 14 patients operated upon for mitral stenosis. Blood samples in each case were taken from the pulmonary artery.

Blood Gas Analysis Using 100% Oxygen by Controlled Respiration

Patient	pH at 37 C	Vol. % CO_2	pCO_2
1	7.478	47.8	27.2
2	7.430	57.6	38.4
3	7.472	53.7	32.0
4	7.562	--	--
5	7.546	57.0	26.4
6	7.592	48.8	22.7
7	7.501	53.9	30.7
8	7.509	41.60	23.6
9	7.550	30.60	22.20
10	7.556	39.18	19.71
11	7.520	43.2	23.54
12	7.423	48.8	32.94
13	7.468	58.0	35.5
14	7.589	56.5	28.3

It seems that very little analgesia is required for the actual surgery on the heart, for once the chest wall is stimulated by the surgeon at the beginning of its closure the patient will respond by movement. This leads one to believe that the heart itself is relatively insensitive to pain from surgical stimulation. We believe that this is for the most part the explanation as to why one may use this particular anesthetic method for cardiac surgery.

Summary

An anesthetic technique using 100% oxygen as the only inhalant during cardiac surgery is described, and an explanation as to why this is possible is presented. The advantages of this method are (1) the impossibility of increase in the depth of anesthesia with controlled respiration, since no inhalant other than oxygen is used; (2) a high oxygen content, with elimination of CO_2; (3) a quiet mediastinum for surgery, and (4) a stable, well-oxygenated heart, which tolerates operative procedures better than when an inhalant anesthetic is used.

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REFERENCES

1. Gerbode, F.: Cardiac Arrest, in Henry Ford Hospital's International Symposium on Cardiovascular Surgery, edited by C. R. Lam, Philadelphia, W. B. Saunders Company, 1955, pp. 396-405.

2. Artusio, J. F., Jr.: Ether Analgesia During Major Surgery, J. A. M. A. 157:33, 1955.

3. Haldane, J. S., and Priestley, J. G.: Respiration, New Edition, London, Oxford University Press, 1935.

4. Rollason, W. N., and Parkes, J.: Anæsthesia, Hyperventilation and The Peripheral Blood, Anæsthesia 12:61, 1957.

5. Crane, M. G.; Affeldt, J. E.; Austin, E., and Bower, A. G.: Alveolar Carbon Dioxide Levels in Acute Poliomyelitis, J. Appl. Physiol. 9:11, 1956.

6. Penrod, K. E.: Nature of Pulmonary Damage Produced by High Oxygen Pressures, J. Appl. Physiol. 9:1, 1956.

7. Penrod, K. E.: Effect of Intermittent Nitrogen Exposures on Tolerance to Oxygen at High Pressures, Am. J. Physiol. 186:149, 1956.

8. Perot, P. L., Jr.; Stein, S. N., and Sonnenschein, R. R.: Relation of Cortical pH to Hyperoxic Convulsions, Am. J. Physiol. 173:158, 1953.

9. Schaefer, K. E.: Oxygen Toxicity Studies in Underwater Swimming, J. Appl. Physiol. 8:524, 1956.

10. Lambertsen, C. J.; Ewing, J. H.; Kough, R. H.; Gould, R., and Stroud, M. W., III: Oxygen Toxicity: Arterial and Internal Jugular Blood Gas Composition in Man During Inhalation of Air, 100% O_2, and 2% CO_2 in O_2 at 3.5 Atmospheres Ambient Pressure, J. Appl. Physiol. 8:255, 1955.

Studies on the Site and Mechanism of Gastrin Release

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Previous studies from this laboratory, as well as elsewhere, have indicated that the antrum of the stomach is the chief or sole source of the gastric-secretion-stimulating hormone, gastrin. Complete excision of the gastric antrum in dogs practically abolishes the secretion of gastric juice from a vagus-denervated Heidenhain pouch.[1] Exclusion of the antrum from the alimentary tract produces a similar reduction in secretion from the Heidenhain pouch, and this is restored if the antrum is replaced in its normal position or transplanted to the duodenum as a diverticulus. Transplantation of the antrum to the colon produces a marked hypersecretion of gastric juice from the Heidenhain pouch. On the other hand, transplantation of similar pouches fashioned from the corpus or fundus of the stomach into the duodenum or colon produces no stimulation of secretion.[2] If the antrum is converted into a vagus-denervated isolated pouch in an animal also provided with a Heidenhain pouch, the introduction of food into the antrum pouch or distention of this pouch produces a profuse secretion of gastric juice from the Heidenhain pouch. This stimulation does not occur if solutions of cocaine or atropine have previously been applied to the antrum mucosa or if the food introduced into the antrum is acid in reaction.[3] Acid applied to the antrum mucosa also prevents the stimulation caused by distention. Solutions of acetylcholine applied to the antrum mucosa likewise cause a profuse stimulation of gastric secretion from the Heidenhain pouch.[4] If gastrin is produced in specific cells in the antrum mucosa, its formation and release could be stimulated by direct contact with certain chemical substances in the food. However, the blocking effect secured by the application of cocaine or atropine to the mucosa suggests that a local nervous reflex is involved, and the release of gastrin secondary to peristaltic activity of the antrum or distention of the antrum suggests that the muscular wall or some of its contained structures play a role in this mechanism. The present experiments were designed to throw light on these questions.

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Experimental Procedure and Results

Heidenhain pouches were constructed in each of six healthy adult mongrel dogs, and each was fitted with a stainless steel cannula brought out through a stab wound to the left of the incision. Each cannula was connected with a rubber bag, and all of the gastric secretion was collected quantitatively each 24 hours. The volume was measured and the free-acid concentration determined by titration with Toepfer's reagent. Milliequivalents of free acid secreted in 24 hours were calculated by multiplying the volume in liters by the free-acid concentration expressed in clinical units.

After the animals had completely recovered from the operation and were eating normally and the secretion from the Heidenhain pouch had become stabilized, the experiment illustrated in Figure 1 was carried out. The design of this experiment was to produce a diverticulum in the colon made up of the muscular walls of the gastric antrum and lined by the mucosa of the colon. Previous work from this laboratory had

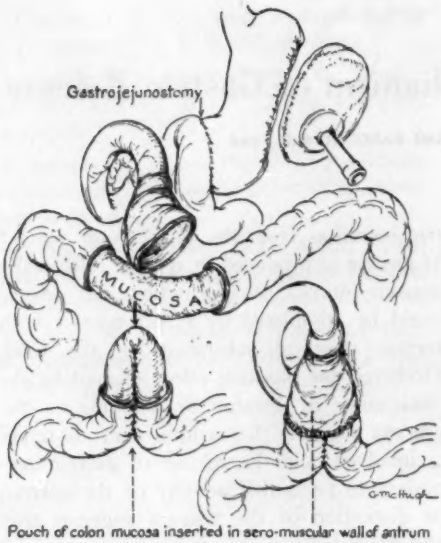

Figure 1

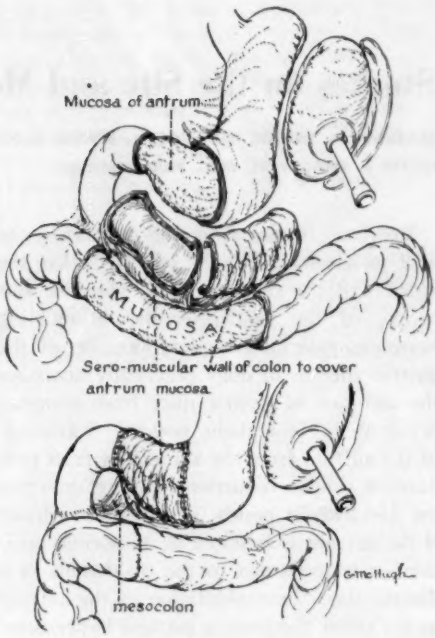

Figure 2

demonstrated that a similar diverticulum made from both antrum mucosa and muscle in their normal relationships causes a profound stimulation of secretion from the Heidenhain pouch. The stomach was transected at the junction between the antrum and the corpus and the mucosa of the antrum excised. At the pylorus the mucosa was infolded and closed. The bare antrum muscle, receiving its blood supply from its attachment to the duodenum, was then transplanted to cover a surgical diverticulum fashioned from the colon mucosa. Gastrointestinal continuity was reestablished by making an anastomosis between the stump of stomach and the side of the first portion of the jejunum. During the control period 39 collections of the 24-hour gastric secretion were secured, with an average volume of 397 cc., 110 clinical units of free-acid, and an average daily output of free hydrochloric acid of 43.7 mEq. After the antrum mucosa had been excised and the colon diverticulum produced, 44 daily collections from the Heidenhain pouch were secured. The average volume decreased to 72 cc., the free acid to 15.4 clinical units, and the average daily acid output to 1.1 mEq. The diverticulum was then excised from the colon, and 51 daily collections of secretion were made. The average volume was 80 cc.; the free acid 72 clinical units, and the acid output 5.8 mEq. It is clear from this experiment that absence of the antrum mucosa prevents the usual stimulating effect on gastric secretion secured by transplantation of the antrum to the colon. Gastrin is not supplied by the antrum muscle lined by colon mucosa.

In the remaining five animals the experiments illustrated in Figures 2 and 3 were performed. In this experiment the antrum muscle was excised and replaced by the muscle of the colon. After the effect of this procedure on the secretion of gastric juice by the Heidenhain pouch had been determined, this hybrid antrum, consisting of antrum mucosa and colon musculature, was transplanted to the transverse colon as a diverticulum. After the effect of this procedure on gastric secretion had been determined, the diverticulum was converted into a closed sac and fitted with a cannula,

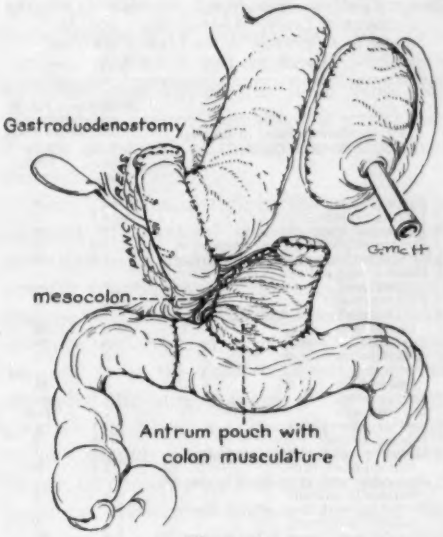

Figure 3

as illustrated in Figure 4. The results of these experiments are summarized in Table 1. In all five of the animals removal of the muscular walls of the antrum and substitution by the muscular coats from the colon produced a marked and sustained reduction in the secretion of gastric juice from the Heidenhain pouch. Thus, in Dog D-168 the

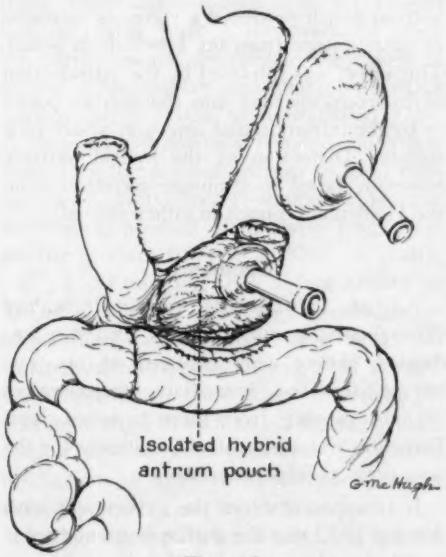

Figure 4

TABLE 1.—*Average Daily Volume, Clinical Units, and Milliequivalents of Free Acid Secreted from the Heidenhain Pouch During a Control Period, Hybrid Antrum Period, After the Hybrid Antrum Had Been Transplanted to the Colon, and After the Animal Had the Antrum Excised or Converted into a Pouch*

Dog No.	Heidenhain Pouch Control Period				Hybrid Antrum				Hybrid Antrum Transplanted to Colon				Antrectomy or Antrum Pouch			
	Ave. Vol., Cc.	Free Acid		No. of Coll.	Ave. Vol., Cc.	Free Acid		No. of Coll.	Ave. Vol., Cc.	Free Acid		No. of Coll.	Ave. Vol., Cc.	Free Acid		No. of Coll.
		Clin. Units	mEq.			Clin. Units	mEq.			Clin. Units	mEq.			Clin. Units	mEq.	
D-168	136	81	11.0	90	64	72	4.6	34	132	108	13.7	37	106	87	9.2	31
D-172	416	117	48.7	55	66	81	5.5	46	D*	D	D	D	D	D	D	D
D-202	672	133	89.4	44	154	98	14.3	30	473	119	56.3	20	D	D	D	D
D-206	161	117	18.8	47	74	61	4.5	32	160	110	21.9	35	82	43	2.2	31
D-280	239	118	28.2	27												
D-52†	397	110	43.7	39					72	15.4	1.1	44	80	72	5.8	51

* Dead.
† D-52 is a different preparation than the others listed.

average 24-hour output of free hydrochloric acid fell from 11.0 to 4.6 mEq.; in Dog D-172, from 48.7 to 5.5 mEq.; in Dog D-202, from 89.4 to 14.3 mEq.; in Dog D-206, from 18.8 to 4.5 mEq., and in Dog D-280, from 28.2 to 6.7 mEq. With the possible exception of Dog D-202, these results are similar to those secured by excision of the antrum. It should be pointed out that in the preparation of this hybrid antrum the colon musculature had been placed around the antrum mucosa in an antiperistaltic direction, the design being to cause stasis of food in the stomach and an optimum opportunity for antrum function. However, when this hybrid antrum was transplanted to the colon as a diverticulum, the average output of hydrochloric acid from the Heidenhain pouch increased markedly in each case. Thus, in Dog D-168 the average 24-hour output of hydrochloric acid increased from 4.6 to 13.7 mEq.; in Dog D-202, from 14.3 to 56.3 mEq.; in Dog D-206, from 4.5 to 21.9 mEq., and in Dog D-280, from 6.7 to 31.2 mEq. It is interesting that the antrum mucosa, when deprived of its normal muscle covering, was functionless in its normal location but active when transplanted into the colon as a diverticulum.

At the conclusion of the experiment, the hybrid antrum was excised from the colon and fitted with a cannula, as illustrated in Figure 4. Only two of the animals, D-168 and D-206, survived this part of the experiment. In D-168 excision of the hybrid antrum from the colon caused the output of free hydrochloric acid from the Heidenhain pouch to decrease from an average of 13.7 to one of 9.2 mEq. per day. Thirty-seven daily collections of daily secretion were secured. In Animal D-206 the average output of hydrochloric acid from the Heidenhain pouch decreased from 21.9 to 2.2 mEq. a day when the hybrid antrum was excised from the colon. Thirty-five daily collections of gastric secretion from the Heidenhain pouch were secured.

The experiments illustrated in Table 2 were then performed on the two animals

TABLE 2.—*Heidenhain Pouch Response to Placing Desiccated Liver, Acetylcholine, and HCl, and to Distention in the Hybrid Antrum Pouch in Dog D-168* *

Test Substance Placed in Isolated Antrum Pouch	Heidenhain Pouch Secretion	
	Vol. for 30 Min., Cc.	Free Acid, Units
1 Fasting control	1	0
2 Fasting control	1.5	0
3 Desiccated liver	2	17
4 Desiccated liver renewed suspension	1.5	14
5 Desiccated liver renewed suspension	1.5	43
6 Pouch rinsed out and N/10 HCl introduced	1 †	Trace
7 Acid renewed	1	0
8 Pouch rinsed out & acetylcholine placed in it	2	22
9 Acetylcholine renewed	5	80
10 Acetylcholine renewed	5	118
11 Pouch rinsed out & N/10 HCl placed in it	2	91
12 Acid renewed	1 †	Acid
13 Acid renewed	1 †	Trace
14 Fasting control	1 †	0
15 Fasting control	1.5	0
16 Distention with 15 cc. of air in the balloon in antrum	1 †	0
17 Distention with 20 cc. of air in the balloon in antrum	1	0
18 Distention with 25 cc. of air in the balloon in antrum	1	0
19 Acetylcholine placed in the antrum	6	61
20 Acetylcholine renewed	7	107
Atropine sulfate, 0.3 mg., intramuscularly		
21 Acetylcholine renewed	2.5	85
22 Acetylcholine renewed	1	Acid
23 Acetylcholine renewed	1.5	34
24 Acetylcholine renewed	1	13
25 Acetylcholine renewed	2	0

* Effect of systemic atropine on the response to local acetylcholine is also shown.
† Less than 1 cc. secretion.

with isolated hybrid antrum pouches, as illustrated in Figure 4. The introduction of liver or solutions of acetylcholine into the antrum pouch produced a vigorous secretion of gastric juice from the Heidenhain pouch. This effect was inhibited by the introduction of hydrochloric acid into the antrum pouch or by the intramuscular injection of atropine sulfate. Distention of the hybrid antrum, however, failed to stimulate secretion from the Heidenhain pouch in either animal.

Comment

All of the animals remained healthy throughout the study periods, except as indicated. Diets were changed at no time except for the immediate postoperative periods, varying from three to seven days. Penicillin was administered routinely for the first three postoperative days.

It is apparent from the experiment with Animal D-52 that the antrum musculature is unable to release gastrin. If it were the site

of gastrin release, its position in this experiment covering a diverticulum of colon mucosa might be expected to produce a hypersecretion of gastric juice from the Heidenhain pouch. Actually, the gastric secretion decreased, as though the antrum had been excised.

Since the musculature of the antrum in a position of maximal stimulation produced no response from the Heidenhain pouch, the reverse situation was prepared. The antrum mucosa was stripped of its overlying musculature and covered with flaps of muscles secured from the colon and placed in an antiperistaltic direction in an attempt to produce stasis in the stomach. This procedure should provide a maximum opportunity to demonstrate an antrum phase of secretion. Somewhat to our surprise, the secretion of gastric juice from the Heidenhain pouch in these animals also decreased in amounts comparable to those produced by antrum resection. There was no tendency of the pouch secretion to return to normal levels, even though the periods of collection lasted several months. Temporary vascular embarrassment can thus be excluded as an explanation for the decrease in secretion. The data in Table 1 demonstrate that in these hybrid-antrum animals a hypersecretion of gastric juice is not produced when the antrum is transplanted to the colon, as occurs with similar transplantation of a normal antrum. Also, as indicated in Table 2, these hybrid antrums respond much less than does the normal antrum to local contact with acetylcholine solutions. In our experience, a small Heidenhain pouch will usually produce from 15 to 30 cc. of gastric juice in 30 minutes, with a free acidity of 120 to 130 clinical units, on the introduction of solutions of acetylcholine into the normal isolated antrum pouch. Removal of the antrum musculature must have traumatized the antrum mucosa to such an extent that greater stimuli were required to activate the gastrin mechanism of the hybrid antrum than are normally present in the dog's stomach.

It thus appeared that neither the antrum muscle nor the antrum mucosa, when separated, was capable of releasing gastrin. However, to make the two preparations as nearly comparable as possible, it was necessary to transplant this hybrid antrum into the colon. Following this procedure, the secretion of gastric juice from the Heidenhain pouch increased to levels roughly comparable to that of the control period (Table 1). This finding demonstrates that the antrum mucosa separated from the antrum musculature can and does release gastrin. Some interference in gastrin release had occurred, or otherwise a hypersecretion of gastric juice from the Heidenhain pouch would have been expected.

Four items seemed to be established by these findings. (*a*) Gastrin is released from one or a combination of structures in the mucosa and submucosa. (*b*) Gastrin can be released in the absence of the antrum musculature and its contained nervous structures. (*c*) The gastrin mechanism remains quite viable and responsive throughout these extensive surgical procedures. (*d*) In order to maintain a normal gastrin mechanism the antrum layers must remain intact.

The profound decrease in gastric secretion caused by removal of the antrum musculature and its substitution by muscle from the colon, and the moderate stimulating effect of transplantation of this hybrid antrum to the colon as a diverticulum prompted the studies summarized in Table 2. In these experiments, solutions of liver and acetylcholine introduced into the isolated hybrid antrum pouch produced vigorous stimulation of gastric secretion from the Heidenhain pouch. This secretion was inhibited by the administration of atropine sulfate or the introduction of solutions of hydrochloric acid into the isolated antrum pouch. It is readily apparent that the antrum responds to most mechanisms of gastrin release and gastrin inhibition. Distention was conspicuously inactive in both animals prepared in this manner. It might be construed that distention releases gastrin by a different mechanism than is required for secretagogues, such as liver and acetylcholine. However, sufficient scarring is seen in the

submucosa of microscopic sections of the hybrid antrum to suggest that it is not possible to distend the mucosa to a sufficient degree. In general, it can be said that the antrum mucosa deprived of the overlying antrum muscularis responds to secretagogues, but not as actively as does the normal antrum in an animal with a denervated pouch. Why not as actively? Little change is seen in the mucosa in microscopic sections. If the cell that produces gastrin is in the mucosa, it might be expected to respond to stimuli in the normal way. If, however, the hypothetical gastrin cell is located in the submucosa, a decreased response might be expected. This area received considerable surgical trauma during the procedure of stripping off the antrum muscle, and there was significant scarring in the submucosa, as revealed in the microscopic sections. It is thus possible that some gastrin cells may have been destroyed and the remainder injured to a greater or less extent. It is probable that Auerbach's myenteric plexus in the antrum and the antrum muscle itself are not the sites of formation or release of gastrin. Could a modified nerve cell, perhaps in Meissner's plexus, be the site of formation and release of gastrin? Several facts support this possibility. A number of hormones are known to be elaborated by modified epidermal structures. Hormonally active modified nerve tissue often exhibits less histological differentiation than other hormonal tissue, such as, for example, the neurohypophysis as compared with thyroid tissue. Finally, the gastrin mechanism can be activated by acetylcholine locally applied and inhibited by the systemic administration of atropine or the local application of anesthetic solutions.

Conclusions

1. The antrum musculature and its contained structures are not necessary for the formation or release of gastrin. 2. Gastrin is formed and released from the mucosa and/or submucosa of the antrum in dogs. 3. The gastrin cell has not as yet been determined, but evidence suggests the possibility that it may be a nerve cell, perhaps in Meissner's plexus. 4. The layers of the antrum must remain intact in order to preserve a normal gastrin mechanism.

Summary

In these experiments, vagus-denervated Heidenhain pouches were prepared in dogs, and the effect of various operations on the antrum on gastric secretion was determined. When the antrum musculature was excised and replaced by musculature derived from the colon, gastric secretion decreased, as though the antrum had been removed. However, transplantation of this hybrid antrum, consisting of antrum mucosa and colon musculature, into the colon as a diverticulum increased the secretion of gastric juice from the Heidenhain pouch toward the normal level. Isolated pouches constructed from this hybrid antrum responded to the introduction of liver solutions or solutions of acetylcholine by vigorous secretion of gastric juice from the Heidenhain pouch. Distention of the hybrid antrum, however, failed to provoke secretion. It is suggested that the cell releasing gastrin may be a modified nerve cell in the submucosa of the antrum.

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REFERENCES

1. Woodward, E. R.; Bigelow, R. R., and Dragstedt, L. R.: Effect of Resection of Antrum of Stomach on Gastric Secretion on Pavlov Pouch Dogs, Am. J. Physiol. 162:99, 1950.

2. Dragstedt, L. R.; Woodward, E. R.; Oberhelman, H. A., Jr.; Storer, E. H., and Smith, C. A.: Effect of Transplantation of Antrum of Stomach on Gastric Secretion in Experimental Animals, Am. J. Physiol. 165:386, 1951.

3. Woodward, E. R.; Lyon, E. S.; Landor, J., and Dragstedt, L. R.: The Physiology of the Gastric Antrum: Experimental Studies on Isolated Antrum Pouches in Dogs, Gastroenterology 27: 766, 1954.

4. Robertson, C. R.; K. Langlois, K.; Martin, C. G.; Slezak, G., and Grossman, M. I.: Release of Gastrin in Response to Bathing the Pyloric Mucosa with Acetyl Choline, Am. J. Physiol. 163:27, 1950.

Gastrectomy Complicated by the Guillain-Barre Syndrome

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Although numerous articles have appeared in the medical literature concerning the various complications encountered after gastric surgery, there has been no report of gastrectomy complicated by the Guillain-Barré syndrome (infectious neuronitis). A careful review of the literature has failed to reveal a single case of this type. The following case is, therefore, reported as an instance of chronic gastric ulcer treated by subtotal gastrectomy in which the Guillain-Barré syndrome appeared as a serious complication, from which the patient subsequently recovered completely.

Report of a Case

History.—A man aged 62 was admitted to the Suburban General Hospital, Dec. 6, 1953, with complaints of epigastric pain, nausea, and vomiting. The pain, which was related to meals, had become intractable during the two months prior to his admission. During this interval, there was a loss of 18 lb. in weight. The past medical history revealed that surgery had been performed Jan. 31, 1950, at another hospital for similar symptoms. A biopsy specimen taken at that time was reported to be diagnostic of a gastric ulcer, and a pyloroplasty was performed.

The patient gave no history of any respiratory infection occurring during the interval preceding his admission.

Examination.—The patient was a small, thin, chronically ill man. Breath sounds were somewhat suppressed at the apex of both lungs. The heart sounds were normal, and no murmurs were heard. The blood pressure was 98 mm. systolic and 64 mm. diastolic. Abdominal examination revealed a transverse curved epigastric scar. There were no other abnormal abdominal findings. The prostate gland was uniformly enlarged.

Laboratory Data.—Blood: red blood cells, 4,210,000; hemoglobin 14.2 gm. per 100 cc.; white blood cells 8200, with 51% polymorphonuclear cells, 48% lymphocytes, and 1% eosinophils. Urine: albumin, trace; sugar, negative; occasional white blood cell. Blood chemistry: nonprotein nitrogen, 33 mg. per 100 cc.; blood sugar, 81 mg. per 100 cc.; sedimentation rate, 6 mm. in one hour. Gastric analysis (histamine stimulation): free hydrochloric acid, 0 degrees (fasting), 24.5 degrees (maximal); total acid, 8 degrees (fasting), 24 degrees (maximal).

Gastrointestinal x-rays were reported to show duodenal deformity and ulcer. The stomach was thought to be free of disease.

Course.—On Dec. 9, 1953, operation was performed under spinal anesthesia, using 14 mg. of tetracaine (Pontocaine) hydrochloride, supplemented with thiopental (Pentothal) and nitrous oxide. Exploration revealed a transverse pyloric scar. There was no evidence of an active ulcer of the duodenum. Along the lesser curvature of the stomach 9 cm. proximal to the pylorus, a small ulcer was found. A subtotal gastrectomy with an antecolic Hofmeister gastrojejunostomy was done.

The early postoperative course was uncomplicated except for urinary retention resulting from the prostatic hypertrophy, with satisfactory response to indwelling catheterization for several days. Ambulation was begun on the second postoperative day. The highest temperature was 38 C (100.4 F). The incision healed by primary intention. Progressive increase in the diet was permitted.

On the ninth day the patient complained of numbness of the left half of his tongue. That same evening, he felt pain across both shoulders and down both arms along the dorsal aspects. This was associated with paresthesia but without other sensory disturbances. The grip of both hands was weak. Reflexes of both upper and lower extremities were active and equal.

On the 10th day pain developed in both thighs, and by the 11th day weakness of both legs was so pronounced that the patient could no longer walk. He complained of numbness in both legs. Reflexes at this time were absent in both the upper and the lower extremities.

On the 12th day neurological consultation was held with Dr. James C. MacLean. A diagnosis of

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Guillain-Barré syndrome was made. This diagnosis was confirmed by the spinal fluid findings of a normal cell count, 3 per cubic millimeter, and an elevated protein, 82 mg. per 100 cc. (normal range, 20 to 40 mg. per 100 cc.).

Therapy, consisting of intramuscular vitamin B and dimercaprol (BAL), was instituted. Despite treatment, the disease continued to progress. There was considerable pain in the hands and feet, and there was evidence of weakness of the muscles of respiration.

On the 14th day the cough reflex was noticeably weak and ineffective. There were increasing respiratory distress and evidence of cyanosis. Swallowing was extremely difficult. Aspiration of the pharynx was required frequently to remove the thick yellow secretions that appeared. That same day the temperature, which had been normal, rose to 38.3 C (101 F).

An emergency tracheotomy was performed under local anesthesia to relieve the acute respiratory distress, and a considerable quantity of thick purulent exudate was aspirated from the trachea. The patient was placed in a Drinker respirator.

Constant nursing care was necessary to ensure frequent aspiration of the tracheotomy tube and to guard against the danger of aspiration in the event of regurgitation from the stomach. Feedings were administered through a nasogastric tube.

On the 16th day paralysis of both legs was complete and weakness of both arms was pronounced. There was considerable pain in both the upper and the lower extremities. Two days later there was some diminution in the pain and slight movement of the extremities was possible. Thereafter there was constant improvement.

On the 23d day respirations had improved to such an extent that it was possible to remove the patient from the respirator and again to resume oral feedings. On the 33d day the tracheotomy tube was removed, and on the 42d day the patient was able to be out of bed for five minutes. He no longer complained of pain in his extremities. Movements of the hands and arms were fairly well coordinated, but there was still moderate weakness of both legs.

On the 47th day the patient was able to walk with the aid of a stroller, and the following day he was able to shave himself for the first time since his illness. The patient was discharged from the hospital on the 50th day, Feb. 7, 1954. At this time he was able to walk about without any assistance; the coordination of movements of his hands was almost normal. Follow-up examination one year after surgery revealed no neurological signs of the previous illness.

Comment

The name Guillain-Barré syndrome has been applied to this syndrome since 1916, when Guillain, Barré, and Strohl described two cases of radiculoneuritis associated with albuminocytologic dissociation in the cerebrospinal fluid. The early cases reported only involvement of the extremities and were followed by recovery. The prognosis was, therefore, considered to be good. Subsequent cases appeared in the literature in which there was evidence of bulbar and cerebral involvement and in which death resulted from the complication.

The etiology of this syndrome is unknown. Blood et al.[1] have suggested that the lesions are allergic in nature. Von Hagen and Baker[2] believe that there is some disturbance in the enzyme metabolism of the neurons due to a toxic or an allergic reaction. This syndrome has been reported in connection with infectious mononucleosis, diphtheria, and porphyria, after various infections, after vaccination for smallpox and Japanese B encephalitis, and with tetanus toxoid. The possible association with spinal anesthesia, as in the case being reported, has not previously been recorded. However, the various neurological complications encountered by Dripps and Vandam,[9] in a study of over 10,000 spinal anesthesias, constitute a picture quite distinct from that of the Guillain-Barré syndrome. The study would tend, therefore, to discount spinal anethesia as an etiologic factor in this syndrome.

In a description of the pathology found in (Landry)-Guillain-Barré syndrome, Karsner[3] reports that there are no evident gross lesions except for hyperemia of the leptomeninges of the cord and the roots. The microscopic lesions are most pronounced in the distal portions of the spinal roots and the proximal parts of the cranial nerves. The initial hyperemia and edema is followed by dissolution of the myelin sheath and, subsequently, by fragmentation of the axis cylinders.

The usual case is characterized by a rather sudden and unexpected onset, preceded often by a mild infection, usually of the respiratory tract. Weakness appears, rather suddenly progressing to paralysis, and is usually associated with hyperesthesia, paresthesia, and anesthesia. Pain is usually severe. Facial nerve paralysis is the commonest of the cranial nerve lesions and occurs in about 50% of cases.

MacNeal [4] has divided the clinical picture into five basic types, depending upon the extent of involvement. These are (*a*) mononeuritic, (*b*) polyneuritic, (*c*) myelitic, (*d*) bulbar, and (*e*) cerebral. The lesions may be ascending or descending, or may become disseminated in no particular sequence.

In those cases in which respiratory paralysis does not develop recovery is the rule. This may be complete or partial. The acute phase usually lasts about one week, following which improvement generally continues until recovery occurs. Some residual disability may persist for weeks, months, or even years.

The albuminocytologic dissociation of the spinal fluid which characterizes this syndrome distinguishes it from similar neurological disorders. Reitman [5] has suggested the following explanation for this dissociation. The basic pathological process consists of an obstruction to the perineural circulation of the cerebrospinal fluid as the nerve roots emerge from the cord, thereby preventing the absorption of the larger protein molecules while permitting the eletrolytes and fluid to be absorbed. Since there is no meningeal involvement, there is no tendency to the development of a leukocytosis in the spinal fluid.

The mortality in those cases manifesting bulbar or cerebral involvement is high, respiratory paralysis being the principal cause of death. Bendz [6] reports a mortality rate of 47% and notes a mortality rate in the literature varying between 15% and 75%. Baker [7] has noted a poorer prognosis in the older age group and reports for patients over 50 years of age a mortality rate as high as 40%. In the older age group the disease tends to be severer, frequently involving the bulbar area.

Treatment of the disease is largely palliative. Blood [1] and Newey [8] report good response to the use of corticotropin (ACTH). Von Hagen [2] has recommended the use of dimercaprol (BAL), in the belief that its use may help to restore enzymatic equilibrium of the neurons. Both he and Bendz [6] emphasize the importance of early tracheotomy, in the hope of reducing the high mortality associated with cases of bulbar paralysis.

Conclusion

A case of chronic gastric ulcer treated by subtotal gastrectomy complicated by the Guillain-Barré syndrome is reported. Although respiratory paralysis and complete paralysis of the upper and lower extremities occurred, the patient survived, and recovery was complete. It is suggested that the early use of a tracheotomy and the respirator were probably the important factors in preventing death in this case.

The subject of the Guillain-Barré syndrome is reviewed. Attention is thereby directed to this syndrome, which heretofore has not been described in the surgical literature.

8114 Jenkins Arcade (22).

REFERENCES

1. Blood, A.; Locke, W., and Carabasi, R.: Guillain-Barré Syndrome Treated with Corticotropin (ACTH), J. A. M. A. 152:139-140, 1953.

2. Von Hagen, K. O., and Baker, R. N.: Infectious Neuronitis, Present Concepts of Etiology and Treatment, J. A. M. A. 151:1465-1472, 1953.

3. Karsner, H. A.: Human Pathology, Ed. 8, Philadelphia, J. B. Lippincott Company, 1955, p. 865.

4. MacNeal, P. S., and Bland, J. H.: The Guillain-Barré Syndrome: Review of Literature; Current Implication and Report of 7 Cases, Am. Pract. & Digest Treat. 1:337-346, 1950.

5. Reitman, N., and Rothschild, K.: The Non-Infectious Nature of the Guillain-Barré Syndrome with a Possible Explanation for the Albumino-Cytologic Dissociation, Ann. Int. Med. 32:923-934, 1950.

6. Bendz, P.: Respiratory Problems in Acute Guillain-Barré Syndrome, A. M. A. Arch. Neurol. & Psychiat. 73:22-27, 1955.

7. Baker, A. B.: Guillain-Barré's Disease in the Older Age Group, Geriatrics 1:132-143, 1946.

8. Newey, J. A., and Lubin, R. I.: Corticotropin (ACTH) Therapy in Guillain-Barré Syndrome, J. A. M. A. 152:137-139, 1953.

9. Dripps, R. D., and Vandam, L. D.: Long-Term Follow-Up of Patients Who Received 10,098 Spinal Anesthetics, J. A. M. A. 156:1486-1491, 1954.

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Indications and Uses for Gastrostomy Tube Suction in Surgery of the Upper Abdomen

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Gastric suction applied through a Stamm gastrostomy catheter has proved to be a very useful and often important adjunct to the postoperative management of certain operative cases. A gastrostomy catheter can be placed through the anterior wall of the stomach, brought out through the upper abdominal wall, and then attached to suction apparatus.

The use of tubes for medical decompression of the stomach dates back to John Hunter.[7,9] Duodenal tubes were first introduced by Turck [13] and Hemmeter [5] (1896). Gastrostomy suction tubes were in use prior to 1930 at the Einar Key Clinic in Stockholm.[12] Among the early advocates of postoperative gastrostomy tube suction in this country was Dr. J. Shelton Horsley,[6] of Virginia, who illustrated its use following Billroth I subtotal gastrectomy (1939). Bisgard [2] (1942) advocated a similar method of jejunal decompression, with the catheter brought out through the stomach wall and down through the gastrojejunostomy stoma following gastric resection. With the use of the double-lumen Abbott-Rawson tube, suction was maintained from the stomach and jejunal feedings given through the jejunal portion of the catheter. Ravdin and others [11] (1943) also used such a postoperative suction feeding device. Allen [1] utilized both a decompressing jejunal catheter and a second gastrostomy catheter postoperatively.

Gastrostomy tube suction is particularly adaptable to the postvagotomy patient, where adequate gastric emptying may be delayed for four or five days and a nasogastric tube will become extremely uncomfortable. This type of direct gastric suction may be indicated postoperatively for patients undergoing portal-caval shunting. It is felt that nasogastric suction is undesirable in such patients postoperatively, since a tube lying across esophageal varices, even for a short time, may cause erosion.

No matter whether rubber or plastic, a nasogastric tube is irritating to the mucous membranes of the nose, throat, and esophagus. In all cases there are an increased mucus secretion and congestion of the respiratory tract. The tube interferes, to a certain degree, with the coughing and clearing of mucus from the tracheobronchial tree, and in the older patients this becomes a hazard. The unhappy experience of patients who have had nasogastric tubes for any length of time is frequently overlooked because use of this type of suction is so commonly a part of postoperative care. Through the use of gastrostomy suction the annoyance of the nasogastric tube is completely eliminated. There is truly a great difference in the appearance and in the comfort of the patient who is decompressed through a gastrostomy catheter rather than the usual Levin tube method.

Although few reviews have been devoted to complications deriving from indwelling nasogastric tubes, serious consequences may develop. The most serious have been esophageal strictures, laryngeal ulceration, and esophageal or gastric perforations. Farris and Smith,[4] who earlier have reported their series of temporary gastrostomy suction tubes, collected a series of 260 complications of nasogastric tubes reported from 59 members of the American Laryngological and American Broncho-Esophagological Associations. From the members responding to

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List of Operative Procedures in Which Gastrostomy Tubes Were Used for Postoperative Gastric Decompression

Operative Procedure	No. of Cases
Billroth I gastrectomy with vagotomy	2
Cholecystectomy (complicated)	2
Cholecystectomy and common-duct exploration	4
Cholecystectomy, choledochotomy, and duodenotomy	5
Congenital jejunal obstruction (newborn)	1
Esophagogastrectomy	2
Exploratory laparotomy (gastric and pancreatic carcinoma)	3
Hiatus hernia repair with esophagitis	3
Islet-cell adenoma resection	1
Pancreatoduodenectomy (Whipple procedure)	3
Portocaval anastomosis	2
Resection of duodenal diverticulum	1
Small-bowel resection with peritonitis	1
Sphincteroplasty (ampulla of Vater)	2
Subtotal gastrectomy: modified Billroth I gastroduodenostomy	2
Total colectomy	1
Vagotomy and pyloroplasty	45
Total cases	80

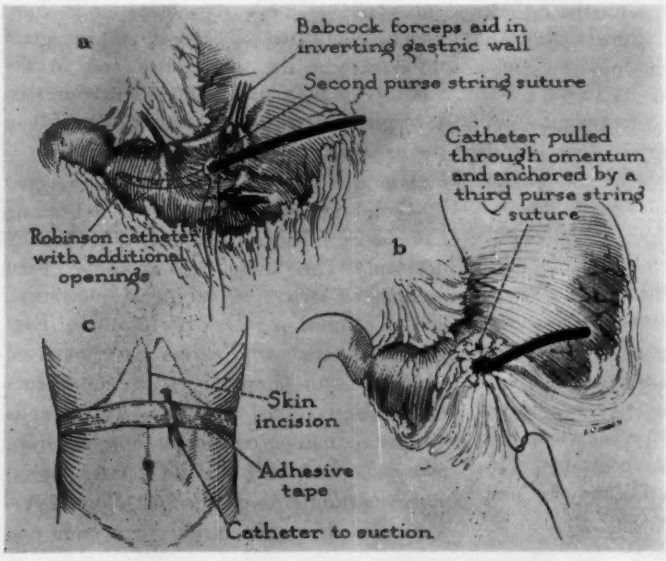
circularized questionnaires a list of 22 esophageal strictures which required dilatation was compiled.

There are also certain advantages which derive from the actual method of suction. The catheter used can be larger in caliber than the usual Levin tube. Since the end of the catheter is introduced directly into the stomach by manual control, it can be placed exactly as desired and then maintained in the position the surgeon wishes. This may be in the dependent portion of the stomach or near a gastrojejunal or gastroduodenal anastomosis. Tubes have frequently been used subsequently as a feeding tube when supplemental feeding seemed indicated.

The tubes may be left in for an indefinite period, but, in the group of cases reported here, were usually discontinued after five to seven days, when the patients had become ambulatory and had demonstrated their ability to take a fairly full diet without retention (Table). Removal of the catheters was completely painless in every instance. The tubes usually could be slipped out without the patient's realizing it. Except for a few drops of fluid immediately accompanying the removal of the tubes, no leak occurred, and a crust was always formed at the end of 24 hours over the stab incision. No symptoms of peritonitis occurred, and there was no evidence of intra-abdominal suppuration or leak. The cases summarized in this report date from 1951, when the use of the gastrostomy suction tube as described here was first suggested by Dr. A. C. Pattison, of Pasadena, Calif.

Operative Technique

Following completion of the primary surgical procedure, the stomach wall is



(*a*) A Robinson catheter is shown in place through the lower anterior gastric wall. (*b*) The tube has been drawn through a flap of gastrocolic omentum and is fixed around the base of the tube with a third purse-string suture. (*c*) The tube is brought out through a separate stab incision in the left epigastric area and fixed in place with a broad band of adhesive around the trunk.

brought up to the anterior wall of the abdomen and a site selected for the gastrostomy which will allow the catheter to be brought out of the abdomen separately from the operative incision. In this group of cases an incision in the midline of the upper abdomen was most frequently used, and the tube was brought out through a narrow stab opening in the left epigastrium (Figure, *c*). Usually an area in the anterior wall of the body of the stomach will be directly under such a stab wound, and this area can be picked up by three lightly placed, smooth Babcock clamps (Figure *a*). A No. 18 straight Robinson catheter is then selected, and additional openings are cut in the distal 3-4 in. of tube. A stab opening is made through the anterior gastric wall and the tube inserted. The stab should go through the mucosa and should not be large so that the tube fits snugly. The tip of the catheter can then be directed toward the pylorus until the operator is satisfied that proper drainage will be obtained. Where duodenostomy has been performed and good decompression is desirable for two or three days to allow for adequate sealing, the distal end of the catheter can be directed through the pylorus for a short distance so that some suction will take place in the upper duodenum.

The catheter is then fixed in place with three successive purse-string sutures of 00 or 000 gastrointestinal gut. The first purse-string suture will hold the wall of the stomach to the catheter, while the second and third sutures will invert tube and wall. With the heavier suture and a soft catheter the suture can be tied too tightly and occlude the lumen. Before placing the third purse-string, the tube is pulled through an opening in an adjacent flap of omentum along the greater curvature of the stomach. The omental flap then is included in the placement of the third purse-string, which is left uncut with the needle still attached (Figure, *b*).

The stab wound for the exit of the tube through the abdominal wall is made and the proximal end pulled through. The entire stomach is then elevated toward the anterior wall of the abdomen, and the remaining suture is used to attach the stomach to the parietal peritoneum at the stab wound exit. The proper tying of this suture results in fixing the base of the gastrostomy to the anterior abdominal wall.

The safest and most satisfactory method of safeguarding the gastrostomy tube in place is taping it to the lower thorax with wide tape (Figure, *c*). The tape can be placed so that respiration is not compromised and yet it will encircle the mid-trunk. In this way it cannot be pulled out by an uncooperative or disoriented patient. This tape should be laid on separately from the main dressing.

If desired, a "sleeper" stitch of cotton or silk can be laid through the edges of the transverse stab incision, to be tied when the tube is discontinued and thus more neatly approximate the edges and lessen the scar.

Summary

The 80 cases in which this method was used between 1951 and 1954 are summarized here: there have been no complications. The tubes have functioned well. In two instances in which the end of the gastrostomy tube was placed too far into the duodenum, the stomach was not decompressed until the catheter was withdrawn from 1½ to 2 in.

The stab incisions closed promptly within a few hours. The patients were far more comfortable than others who had nasogastric tubes. Respiratory complications were less than in a comparable group of patients with nasogastric tubes. Among these patients were several who had previously been on conventional suction and were particularly appreciative of the difference. There were no complications from the use of the gastrostomy tube.

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REFERENCES

1. Allen, A. W., and Donaldson, G.: Jejunostomy for Decompression of the Postoperative Stomach, Surgery 15:565-568 (April) 1944.

2. Bisgard, J. D.: Gastrostomy—Jejunal Intubation, Surg. Gynec. & Obst. 74:239-241 (Feb.) 1942.

3. Eade, G. G.; Metheny, D., and Landmark, V. O.: An Evaluation of the Practice of Routine Nasogastric Suction, Surg. Gynec. & Obst. 101: 275-279 (Sept.) 1955.

4. Farris, J. M., and Smith, G. K.: An Evaluation of Temporary Gastrostomy—A Substitute for Nasogastric Suction, Ann. Surg. 144:475-486 (Sept.) 1956.

5. Hemmeter, J. C.: Intubation of the Duodenum, Bull. Johns Hopkins Hosp. 7:79-80 (April) 1896.

6. Horsley, J. S.: Peptic Ulcers Perforating into Pancreas, Ann. Surg. 110:606-621 (Oct.) 1939.

7. Hunter, J.: A Case of Paralysis of the Muscles of Deglutition Cured by an Artificial Mode of Conveying Food and Medicines into the Stomach, in The Complete Works of John Hunter, edited by J. F. Palmer, Philadelphia, Haswell, Barrington & Haswell, 1841, Chap. 3, p. 580.

8. Iglauer, S., and Molt, W. F.: Severe Injury to the Larynx Resulting from Indwelling Duodenal Tube: Case Reports, Ann. Otol. Rhin. & Laryng. 98:886-904 (Dec.) 1939.

9. Paine, J. R.: The History of the Invention and Development of Stomach and Duodenal Tubes, Ann. Int. Med. 8:752-763 (Dec.) 1934.

10. Pattison, A. C.: Personal communication to the author.

11. Ravdin, I. S.; Royster, H. P.; Riegel, C., and Rhoads, J. E.: Surgical Care of Patients with Gastric Cancer Before and After Operation, Arch. Surg. 46:871-878 (June) 1943.

12. Schmidt, E., cited by Alton Ochsner, in commenting on paper by Farris and Smith.[4]

13. Turck, F. B.: The Improved Gyromele, New York M. J. 63:191 (Feb.) 1896.

Use of Randall Forceps in Bile Duct Surgery

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In 1932 Alexander Randall, of Philadelphia, described a set of four forceps which he had devised for the removal of calculi from the renal pelvis.[1] These instruments may be employed to great advantage in removal of choledochal stones and in exploration and manipulation of the bile ducts and ampulla. Their adaptability to this type of surgery, however, is apparently not generally appreciated. The object of this report is to call attention to the advantages of the Randall forceps in bile duct surgery. In addition, a fifth clamp will be described, representing a slight modification of the Randall forceps, intended to supplement, but not to replace, the conventional set.

The four Randall forceps may be found in the surgical equipment of most hospitals; however, they are customarily classed as urological rather than as general surgical instruments. The set consists of four grasping forceps, similar to one another in length and general construction, but varying in curvature to permit access to the upper, intermediate, and lower calyces through a pyelotomy or nephrotomy incision (Fig. 1). The outer edges are beveled to prevent damage to mucous membranes, while the opposing surfaces are recessed and serrated to increase their grasping function.

The No. 1 instrument is slightly curved. Its design is similar in most respects to that of the Desjardin, Blake, or Mayo gallstone forceps which are in common use. However, in the catalogues of various surgical instrument makers the forceps described for choledocholithotomy are usually either straight or only slightly curved. Nowhere under the listing of gallbladder instruments can one find grasping forceps with as much as a 90-degree curve. Yet it is often desirable or necessary to bend probes, dilators, or scoops into curvatures considerably in excess of that. The curvatures afforded by the Randall forceps represent a range varying from a slight curve, in the No. 1 instrument, to an approximate half-circle, in the No. 4 instrument, and thus are comparable to the curvatures which can be achieved by bending flexible dilators and probes.

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Fig. 1.—Set of Randall forceps.

In his original report Dr. Randall stated that "calculi have most fickle habits when in the renal pelvis, and to win, one has to woo them, at times, with every art and artifice." This statement could be applied to choledochal stones as well. In the removal of choledochal stones, the range of curvatures of the Randall forceps affords access to all major parts of the bile duct system. The No. 1 clamp, with its gentle curvature, is ordinarily selected for exploration of the right and left hepatic ducts, while the No. 2 clamp is useful in the proximal portion of the common bile duct. Either the No. 3 or the No. 4 clamp is used in the distal and ampullary portion of the duct, depending upon individual variations in the degree of ductal curvature.

In addition to their function purely as grasping instruments, the Randall forceps have proved to be of great value for exploration and manipulation of the duodenal ampulla. Determination of patency of the ampulla is frequently the most difficult prob-

lem encountered during operations upon the bile ducts. The sphincter is likely to contract during anesthesia or manipulation, and the ampulla tends to evert into the duodenum in advance of the conventional dilator, rather than yielding to it. Pronounced degrees of curvature of the distal portion of the duct impose an additional technical difficulty, making it necessary to apply the dilating force in a sweeping curve. In the course of an otherwise normal exploration of the bile ducts, or after all choledochal stones have presumably been removed, the surgeon is often confronted with the discovery that his probe or dilator has failed to enter the duodenum. In the absence of duodenotomy, proof that the instrument has entered the duodenum can be established only by being able to see the metal of the instrument shining through the duodenal wall. When the instrument is at the ampulla but has not traversed it, it is usually possible to feel the tip through the near and far walls of the duodenum. The application of force in such instances is likely to result in false passage. When ordinary manipulations fail to establish proof of patency of the ampulla, one is left with the alternative of performing duodenotomy or operative cholangiography or of making the hazardous assumption that the ampulla is merely in a state of spastic contracture. It is here that the Randell forceps have proved especially useful. The instrument with the appropriate curvature is introduced in the duct and passed distally until the tip everts the ampulla into the duodenum; the jaws of the clamp are then opened and closed several times while a gentle everting force is still applied. This serves to overcome any spasm of the ampullary sphincters, and the operator is usually gratified to see the head of the clamp suddenly pop through into the duodenum. Thereafter the metallic shine of the instrument is clearly visible through the intact duodenal wall (Fig. 2). It is probable that this maneuver may overcome some contractures of the ampulla on occation. After the first passage it is usually easy to introduce probes and dilators. If

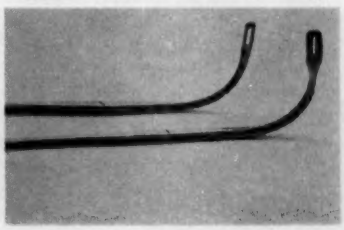
Fig. 2.—Randall forceps passed down bile duct, through ampulla, and into duodenum. Tip visible through duodenal wall.

desired, the Randall forceps may be employed to pass a catheter or Cattell tube into the duodenum. I have abided by the rule always to perform duodenotomy unless it was certain that the exploring instrument had entered the duodenum. Since the use of the Randall forceps has been adopted, the necessity for duodenotomy has declined greatly.

It is occasionally desirable to employ an instrument with a broader grasping surface to deal with larger stones or multiple stones. For this purpose I have designed a modification of the Randall forceps similar in all respects to the standard instruments but having a head approximately twice as large * (Fig. 3). The curvature of this clamp is approximately 90 degrees. It is used only occasionally to supplement the conventional set of four, and is in no sense intended to replace them. The small head of the standard instrument may occasionally slip past a small stone in a greatly dilated duct; this

* This instrument was prepared to specifications by V. Mueller & Company, of Chicago.

Fig. 3.—Author's supplementary instrument compared with standard No. 2 Randall forceps.



is less likely when the supplementary instrument with the larger head is used.

Summary

Randall forceps, designed for pyelolithotomy, may be employed to great advantage in surgery of the bile ducts. The set of four instruments is available in most hospitals. Their utilization in biliary surgery is described. A modified clamp with a larger head has been designed to supplement the standard set.

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REFERENCE

1. Randall, A.: Improved Forceps for the Removal of Renal Calculi, S. Clin. North America 12:1501 (Dec.) 1932.

Autotransplantation of the Lingual Thyroid

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When the medial anlage of the thyroid gland fails to descend into the neck from its point of origin in the oropharynx, a lingual (accessory) thyroid results. In 1936 Montgomery [1] proposed standard criteria for the diagnosis of this anomaly: (*a*) location of the aberrant tissue at the base of the tongue between the circumvallate papillae and the epiglottis, (*b*) microscopic demonstration of thyroid tissue, and/or (*c*) development of hypothyroidism following removal of the lesion. Subsequently, recognition of the lingual thyroid has been greatly facilitated by radioiodine tracer techniques, so that, in practice, concentration of I^{131} by such a lesion is now considered adequate evidence for the diagnosis.

While diagnosis has been greatly simplified, the problem of treatment has stimulated some debate. Several therapeutic measures have been employed, including suppression with inorganic iodine, ablation with radioiodine, subtotal resection, and total excision. Medical therapy with inorganic iodine has been employed in so few recorded cases that it cannot properly be evaluated, but it seems highly doubtful that such treatment could be permanently effective in many cases. Partial or total destruction of the lesion by radioiodine has been accomplished,[2,3] but the use of this agent, with its unknown cancerogenic potential, is presently undesirable in the young age group in which this lesion is usually encountered. Surgical removal appears to be the treatment of choice in most patients. Because complete removal of the lingual thyroid usually produces hypothyroidism, subtotal excision has often been recommended.[4,5] But resection of sufficient tissue to relieve obstructive symptoms has, in fact, also produced hypothyroidism with considerable frequency. In our view, the basic consideration in the treatment of this lesion is the belief that thyroid tissue at the base of the tongue is fundamentally undesirable. Therefore, we believe that total excision should be carried out.

Following total removal of the lesion, substitution treatment must be provided in almost all cases. Replacement therapy with thyroid extract, thyroxin, or triiodothyronine is eminently successful. Its disadvantages are the minor ones of cost and the need for faithful administration. On the other hand, it is apparent that all endocrine substitution therapy by exogenous hormone administration is partially defective in that the supply of hormone cannot be concisely correlated with varying hormone requirements. The ideal solution would appear to lie in hormone replacement by the transplantation of endocrine tissue, on the assumption that a successful transplant should function in response to normal stimuli. While this problem is of much greater significance to the welfare, or even survival, of patients with adrenal cortical insufficiency or hypoparathyroidism, the same consideration must also apply, in some degree, to the treatment of myxedema. Consequently, the total excision of a lingual thyroid affords an excellent opportunity for the study of permanent "substitution therapy," since the autografts should survive in a high proportion of cases.

Two patients with lingual thyroid have been encountered at Colorado General Hospital. The first patient, reported in 1952,[6] underwent total excision of the lesion, fol-

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lowed by a rapidly improvised attempt at autotransplantation. The latter was partially successful in that function could be demonstrated by the concentration of radioiodine in the autografts. However, hormone secretion was inadequate for the maintenance of euthyroidism, and eventually the administration of thyroid extract was required. Subsequently, experimental studies in this laboratory[7] resulted in standardization of surgical techniques required for successful thyroid transplantation, so that we were better prepared to undertake this procedure again when the second case of lingual thyroid was encountered, in 1954. This report describes the procedure employed in the latter patient and the results observed over the subsequent three years.

Report of a Case

A 7-year-old girl was admitted to the hospital in October, 1954, because of a mass at the base of the tongue. The lesion had been discovered during a regular public school physical examination. The child had no complaints. No previous illnesses had occurred except rubella, without complications, at the age of 4 years. Both parents are living and well, and four male siblings are healthy.

Physical examination disclosed an alert, well-nourished girl. Her height was 45 in. (114 cm.), and her body weight was 44 lb. (20 kg.). Both measurements are significantly below average for the patient's age. Temperature, pulse, and respiration were normal. The blood pressure was 105 mm. Hg systolic, and 74 mm. Hg diastolic. Her capacity for physical activity appeared to be normal, and while at play there was no dyspnea. Both solids and liquids could be swallowed without difficulty. The voice was normal. A dusky-red mass, approximately 2 cm. in transverse diameter, was present on the base of the tongue behind the circumvallate papillae and covering the normal site of the foramen cecum. It was hemispherical in shape, fitting neatly beneath the inferior curved margin of the soft palate, so that the tip of the uvula lay on the midline of its superior surface. The mass was moderately firm to digital palpation, with an elastic consistency, and its base was firmly embedded in the tongue. Numerous dilated veins coursed over its smooth surface. In the neck, no thyroid gland could be felt. Otherwise, physical examination was normal.

Laboratory examination disclosed a hemoglobin of 12 gm. per 100 cc. and a white cell count of 8700 per cubic millimeter, with a normal differential pattern. Urinalysis was normal. Serum total cholesterol was 167 mg., with cholesterol esters of 124 mg., per 100 cc. The protein-bound iodine was 4.2 mg. per 100 cc. Following a tracer dose (8μc) of radioiodine, all detectable radioactivity emanated from the base of the tongue and no activity could be detected over the normal location of the thyroid gland in the neck. Lateral x-ray films of the skull demonstrated a mass at the base of the tongue almost impinging upon the posterior wall of the pharynx. A diagnosis of lingual thyroid appeared firmly established. Unfortunately, skeletal age was not determined, but, despite the patient's small size, she was considered to be euthyroid. It is of some interest that the child's four brothers all showed comparable growth retardation relative to chronologic age.

Because of the size and vascularity of the mass, threatening oropharyngeal obstruction, total excision was decided upon, and transplantation of the excised tissue was selected as the procedure of choice for providing permanent "substitution therapy." Removal of the lingual thyroid was carried out through a transhyoid cervical approach. A transverse incision was made just below the hyoid bone. The strap muscles were cut, and the incision was developed to the hyoid, which was then cleared of its muscular insertions approximately 1 cm. to each side of the midline. The stripped portion of the bone was then excised. The incision was continued through the hyoid muscles until the lingual mass, pushed anteriorly and downward through the mouth by the anesthetist, was encountered. The mass was firmly encapsulated. Dissection then proceeded posteriorly to the pharnygeal wall. The tumor was dissected free from the musculature of the tongue and removed intact. In order to avoid contamination, the mass was not weighed. On the basis of comparison with normal thyroid tissue of approximately equal size, the weight was estimated to be 1.5 to 2.0 gm. The mass was washed thoroughly in Ringer's solution, and, using clean instruments, the fibrous capsule was stripped away, exposing normal thyroid tissue. One small piece was removed for examination by the pathologist, and the remainder was cut into slices approximately 2 mm. in thickness. Two vertical incisions were then made in the abdominal wall approximately 1 in. to either side of the umbilicus and approximately 3 in. in length. These incisions were carried down to the anterior rectus fascia, and the rectus muscles were split throughout the length of the incisions. Six thyroid slices were implanted intramuscularly in the right incision; five slices were similarly implanted on the left (Fig. 1). The abdominal incisions were then closed with interrupted silk sutures. Finally, the neck incision was

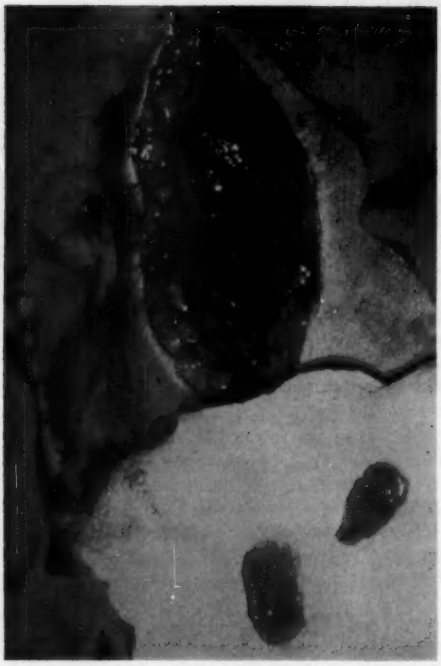

Fig. 1.—Operative photograph, showing two thin slices of the patient's thyroid gland just before insertion into the rectus muscle.

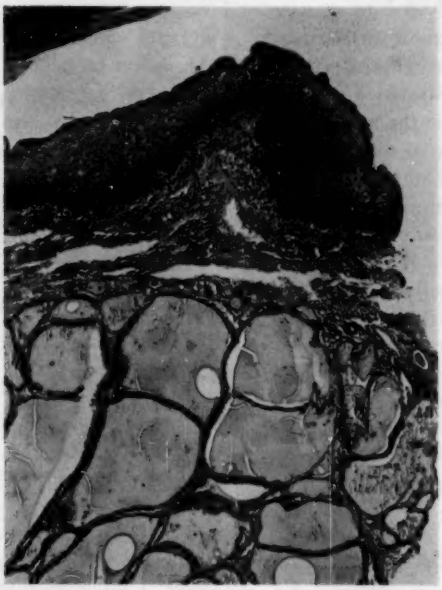

Fig. 2.—A photomicrograph of the lingual edge of the gland, showing normal thyroid follicles lying beneath the mucosa of the tongue.

closed anatomically with interrupted silk sutures, and a drain was left in the center portion of the wound. The patient left the operating room in excellent condition. Penicillin was given intramuscularly, 800,000 units daily, on the day of operation and for seven days postoperatively. The patient had fever (temperature to 38 C) for four days following operation, with a moderate degree of tachycardia. Thereafter, the postoperative course was completely uneventful, and the patient was discharged on the 11th postoperative day. Biopsy showed normal thyroid tissue (Fig. 2).

Following discharge from the hospital, no medications were administered. Initially, there were a gradual decrease in appetite, a moderate decline in physical activity, and some dryness and scaliness of the skin. However, four months after transplantation the 24-hour radioactive iodine uptake (tracer dose: 7μc) counted over the abdominal incisions was 17% and the 24-hour I^{131} conversion ratio was 11%. Unfortunately, serum submitted at this time for protein-bound iodine determination was lost. Nevertheless, despite clinical manifestations of mild hypothyroidism, the transplanted thyroid was definitely functional four months following excision and grafting. During the next six months all symptoms of hypothyroidism, with the exception of some excessive dryness of the skin, disappeared. Nine months after transplantation, the serum protein-bound iodine was 5.2 mg. per 100 cc. Two years after surgery the protein-bound iodine was 5.6 mg. per 100 cc., and, following a tracer dose (8μc) of radioiodine, 24-hour uptake measured over the abdominal incisions was 24%, with a 24-hour I^{131} conversion ratio of 16% and a protein-bound I^{131} of 0.17% of the administered dose per liter of plasma. All of these indices are normal.

Complete evaluation of the child was again carried out three years after thyroid transplantation, at 10 years of age (Fig. 3). Her height was 49.5 in., (125 cm.) and her weight was 57 lb. (25.9 kg.). Although her height-age was only 7 years, both height and weight had continued to increase following operation, so that her growth curve remained almost linear. However, x-ray films of the long bones showed that long-bone length and bone age were well below chronological age, and were approximately average for a 6- to 7-year-old girl. No disproportion or abnormality of the long bones was present. The child had performed satisfactorily (B average) in school. Physical activity was normal. Her hair was soft and fine. Her skin was dry and somewhat hyperkeratotic over the extensor surfaces of the arms, but elsewhere it was normal. Her pulse was regular, at a resting rate of 78 per minute. Blood pressure was 110 mm. Hg systolic and 80 mm. Hg diastolic. No residual thyroid tissue could be seen at the

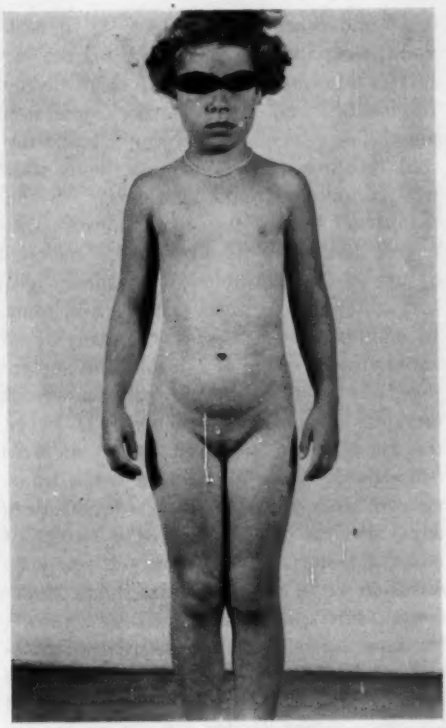

Fig. 3.—A photograph of the patient, age 10 years. Her height is 49.5 in. and the weight 57 lb. (normal for a child of 6 years).

base of the tongue. The neck and abdominal incisions were well healed.

The serum protein-bound iodine was 3.9 mg. per 100 cc. Following a tracer dose (34 μc) of radioiodine, the amounts of radioactivity in the two paramedian abdominal incisions were approximately equal. Counting rates in the oropharynx and over the neck were essentially equivalent to those obtained over the thigh, indicating the absence of significant residual thyroid tissue at the base of the tongue or in the neck. A 24-hour radioiodine uptake, measured over the abdominal incisions, was 30%, with a 24-hour I^{131} conversion ratio of 30% and a protein-bound I^{131} of 0.13% of administered dose per liter of plasma. As before, all of these values were normal.

In order to evaluate thyroid reserve function, 10 U. S. P. units of thyroid-stimulating hormone (TSH) was then administered intramuscularly on each of two successive days. On the second day, following a background count over the autograft sites, a second dose (25μc) of radioiodine was given. The 24-hour uptake failed to increase above the previous control measurement. Similarly, the protein-bound iodine also failed to show a significant rise. Thus, despite essentially normal indices of thyroid function, it must be concluded that the total mass of functioning thyroid transplant was inadequate to provide a normal thyroid reserve.

Comment

When a patient with a lingual thyroid exhibits dysphagia, dysphonia, or dyspnea, or has had episodes of hemorrhage, or has developed cancer, the need for treatment is obvious. Not so obvious is the decision in the case of a young patient who is essentially free of symptoms. Unfortunately, the natural course of this disorder is not well known, since there are few reports in the literature of patients followed over long periods without therapeutic intervention. Nevertheless, available evidence indicates that the majority of patients who harbor this lesion will eventually develop obstructive symptoms, usually relatively early in life. Therefore, it is our feeling that the potential for distressing or threatening sequelae is so great that treatment, preferably by complete removal, is indicated in children and young adults irrespective of symptoms.

The recommendation that an asymptomatic lesion be treated requires that the treatment be safe. In the past, most patients undergoing resection of the lingual thyroid have been operated upon via the oral route, and the majority of these procedures have been carried out without complications. However, in some cases adequate exposure could not be obtained and serious hemorrhage and respiratory difficulties resulted. Emergency tracheotomy and ligation of the lingual arteries or of the external carotids have occasionally been necessary. On the other hand, the transhyoid approach appears to be much more satisfactory, since it provides superior exposure and control of hemorrhage and protection of the airway can readily be achieved. Alternatively, a lateral pharyngeal approach appears to offer equally good results.[8] With either of the latter two procedures, the resection of a lingual thyroid can probably be achieved at a risk rate comparable to that of the excision of

a thyroglossal-duct cyst. This degree of safety provides justification for the belief that an accurate diagnosis of the lingual thyroid constitutes an adequate indication for its removal.

At the same time, the safety of transplantation must also be considered. The insertion of small tissue slices into the rectus abdominis muscles involves no real technical hazard, provided infection is avoided. On the other hand, Ward et al.[8] have suggested that transplantation of the lingual thyroid is fundamentally hazardous because of the possibility of eventual thyroid cancer in the transplant. This opinion is based on the conclusive demonstration of carcinoma of the lingual thyroid in at least six recorded cases. Numerous reports are available to show that the lingual thyroid is subject to the same pathologic changes as thyroid tissue in the normal cervical position, with the possible exception of lesions leading to hypothyroidism.[4] That thyroid tissue in any location may potentially develop carcinoma would appear to be self-evident. That it does so with greater frequency in ectopic tissue than in the normally located thyroid gland has not yet been established. If an abnormally high rate of malignant change in the lingual thyroid can be shown, it seems obvious that transplantation is hardly advisable. On the other hand, if carcinoma actually occurs with no greater relative frequency in the lingual gland than in the cervical gland, then Ward's recommendation against transplantation is really no more reasonable than a recommendation that all thyroid glands be removed for the purpose of prophylaxis. As stated above, the natural course of the lingual gland is not yet adequately documented, so that the true risk involved in autotransplantation of the lesion cannot be evaluated.

Three previous attempts elsewhere at autotransplantation of the lingual thyroid have been described.[9-11] Unfortunately, all failed. Experimental studies relating to the problem of thyroid autotransplantation in animals have previously been reported from this[7] and other laboratories.[12-14] In addition, Szilagyi et al.[15] have recorded the successful autotransplantation of small thyroid fragments into the sternocleidomastoid muscles of patients undergoing subtotal thyroid resection. Thyroid tissue lends itself well to autografting. Avoidance of contamination during transplantation is paramount and is, in all likelihood, facilitated by use of the transhyoid or parapharyngeal surgical approach rather than the oral route. In addition, the present-day availability of antibiotics provides a valuable aid not enjoyed by those who originally undertook therapeutic autotransplantation. However, the fundamental technical factor involved concerns the shape of the piece to be transplanted, since, for a period of at least several days, survival depends upon the receipt of nutrient materials and of oxygen solely by diffusion from the interstitial fluids immediately surrounding the graft. Therefore, maximal surface area is essential. This is best achieved by the use of very thin (1 to 2 mm.) slices of tissue.[7] The length and breadth apparently are not important, but thickness is certainly critical. We have termed this method the "bread-slice" technique. We believe the method was important in the success achieved in this patient. In addition, recently another successful autoimplantation of thyroid in this fashion has been reported by Lawson.[16]

Finally, a decision must be made concerning the optimal area for transplantation. The following characteristics of the transplant site have been considered: (*a*) The recipient bed must be maximally favorable for the survival of the graft. Experimentally, successful transplantation has been achieved in subcutaneous tissue, the peritoneal space, muscle, liver, spleen, and brain. (*b*) The site should afford some protection from subsequent trauma. On this basis, subcutaneous tissue should probably not be employed. (*c*) The area should be relatively superficial, so that tactile and visual examinations may be made. This requirement is not met by either brain or the peritoneal

space. (*d*) Venous drainage of the transplant site should not flow directly to the liver, where metabolism and excretion of the thyroid hormone are known to occur. Consequently, neither the spleen nor the liver itself is suitable. (*e*) The site of transplantation should be subject to easy total excision in the event that disordered function or structure of the graft might in the future require its removal. (*f*) The implantation scar should be cosmetically acceptable. The best approach to these criteria appeared to be offered by the rectus adbominis muscle. Consequently, this site was selected for clinical trial in the patient recorded here.

The functional state of the autograft was evaluated by frequent observations on the clinical status of the patient and by serial measurements of serum protein-bound iodine and the fate of tracer doses of radioiodine. Because of potentially damaging effects, radioiodine was sparingly used in the early postoperative period. Although clinical signs of mild hypothyroidism were evident during the second month following transplantation, gross manifestations of thyroid deficiency did not occur. Therefore, it seems probable that the graft exhibited some degree of secretory function relatively soon following transplantation. Moreover, four months after surgery the uptake of radioiodine and its conversion to protein-bound radioactive iodine were essentially normal. This is in contrast to the first case, previously reported from this clinic,[6] in which autotransplantation of a lingual thyroid was carried out. In that case a significant concentration of radioiodine in the autograft could not be demonstrated until approximately seven months after transplantation. However, studies in rats, rabbits, and mice [12-14] have shown that thyroid autografts exhibit an almost continuous uptake of radioiodine except for a brief interval of four to six days prior to revascularization, before tissue regeneration overcomes ischemic necrosis. Furthermore, Szilagyi et al.[15] demonstrated definite concentration of radioiodine in human thyroid autografts (following subtotal resection of the cervical thyroid gland) as early as 10 days following transplantation.

Since the main objective of transplantation was to provide a regulated supply of thyroid hormone commensurate with the metabolic needs of the patient, the capacity of the autograft to maintain euthyroidism and the relationship of the graft to anterior pituitary function (TSH secretion) were of primary interest. That the serum level of protein-bound iodine, the uptake of radioiodine, and the conversion of inorganic radioactive iodine to serum protein-bound radioiodine are all normal three years after transplantation surely indicates that the autografts are functioning and are responsive to endogenous thyroid-stimulating hormone. On the other hand, the child shows definite retardation of growth and delayed skeletal development. Thus, although epiphyseal dysgenesis is absent and bodily proportions are normal, it is quite probable that thyroid hormone production is below that required for normal growth.

The normal thyroid in infancy weighs approximately 1.5 to 2.0 gm.; that of the adult, approximately 30 gm., the difference reflecting the fact that with body growth and maturation the maintenance of euthyroidism normally entails proportionate thyroid growth. In the present case the estimated weight of the excised lingual thyroid was 1.5 to 2.0 gm., when the child was 7 years of age. It is highly probable, from the behavior of autografts in animals, that at least some of the transplanted tissue promptly underwent necrosis, so that the quantity of surviving tissue must have been less than that actually transplanted. Therefore, the total mass of functioning thyroid transplant must have been materially less than that of a normal 7-year-old child. It is well known that a relatively small quantity of thyroid tissue remaining after subtotal resection or after partial ablation by radioiodine can, in some instances, maintain clinical euthyroidism and essentially normal

laboratory indices of thyroid function by intense hyperplasia resulting from maximal stimulation by endogenous thyroid-stimulating hormone.[16] The failure of the autografts in this child to respond to administered TSH suggests that the transplants are now functioning at maximal capacity (low thyroid reserve). Therefore, it would appear that the comparatively small quantity of tissue which was transplanted has not undergone significant growth, or at least has not attained a total mass sufficient to maintain euthyroidism. It seems highly probable that the capacity of thyroid transplants to sustain normal development, maintain euthyroidism, and still possess demonstrable reserve function is, to a large degree, determined by the absolute quantity of tissue which survives transplantation.

Summary

A lingual (accessory) thyroid in a 7-year-old girl was treated by total excision carried out through a transhyoid approach. Successful autotransplantation of the excised thyroid tissue into the rectus abdominis muscle was achieved. Subsequent observation over a period of three years has demonstrated that the autografts function under the controlling influence of the anterior pituitary gland. However, thyroid reserve is low, indicating that the capacity of the transplanted thyroid tissue to regenerate and grow is not unlimited.

Mr. Arnold Feldman, Department of Radiology, carried out the diagnostic and follow-up studies with radioiodine, and Dr. Marion Maresh, of the Child Research Council, interpreted the x-rays for bone age.

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REFERENCES

Montgomery, M. L.: Lingual Thyroid—Comprehensive Review, West. J. Surg. 43:661, 1935; 44: 54, 122, 189, 237, 303, 373, 442, 1936.

2. Schilling, J. A.; Karr, J. W., and Hursh, J. B.: Treatment of a Lingual Thyroid with Radioactive Iodine, Surgery 27:130, 1950.

3. Nachman, H. M.; Crawford, V., and Bigger, I. A.: Radioactive Iodine, I^{131}, in the Diagnosis of Lingual Thyroid, J. A. M. A. 140:1154, 1949.

4. Goetsch, E.: Lingual Goiter: Report of 3 Cases, Ann. Surg. 127:291, 1948.

5. Rundle, F. F., Editor: Joll's Diseases of the Thyroid Gland, Ed. 2, New York, Grune & Stratton, Inc., 1951, p. 303.

6. Swan, H.; Harper, F., and Christensen, S. P.: Autotransplantation of Thyroid Tissue in the Treatment of Lingual Thyroid, Surgery 32:293, 1952.

7. Liddle, E. B.; Wittenstein, G. J., and Swan, H.: Studies on Autotransplantation of Thyroid and Adrenal Gland in Dogs, S. Forum (1953) 4:701-705, 1954.

8. Ward, G. E.; Cantrell, J. R., and Allan, W. B.: The Surgical Treatment of Lingual Thyroid, Am. Surgeon 139:536, 1954.

9. Buckman, L. T.: Lingual Thyroid, Laryngoscope 46:765, 878, 935, 1936.

10. Ray, B. S.: Lingual Thyroid, Arch. Surg. 37:316, 1938.

11. Wapshaw, H.: Lingual Thyroid: A Report of a Case with Unusual Histology, Brit. J. Surg. 30:160, 1942.

12. Woodruff, M. F. A., and Woodruff, H. G.: Transplantation of Normal Tissues, with Special Reference to Auto- and Homotransplants of Thyroid and Spleen in the Anterior Chamber of the Eye, and Subcutaneously in the Guinea Pig, Phil. Tr. Roy. Soc. London 234:559, 1950.

13. Bennett, D., and Gorbman, A.: Reestablishment of Function in Transplanted Thyroid Glands in Mice, Endocrinology 49:310, 1951.

14. de Pasqualini, C. D., and Mancini, R. E.: Greffe de thyroïde dans le rate, Compt. rend. Soc. biol. 145:1719, 1951.

15. Szilagyi, D. E.; Barrett, J. L.; Longabaugh, E. R., and Preuss, L. E.: A Radioiodine Tracer Study of the Fate of Human Thyroid Autotransplants, J. Clin. Endocrinol. 13:1347, 1953.

16. Lawson, R. S.: Case of Lingual Thyroid with Successful Grafting After Operative Removal, Australian & New Zealand J. Surg. 26:241, 1957.

17. Jefferies, W. McK.; Kelly, L. W., Jr.; Levy, R. P.; Cooper, G. W., and Prouty, R. L.: The Significance of Low Thyroid Reserve, J. Clin. Endocrinol. 16:1438, 1956.

Case Reports

Removal of a Foreign Body in the Rectosigmoid Using a Tonsil Snare

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Foreign bodies are introduced through the anus, either through impalement or from a therapeutic mishap.[1] Among the latter are such items as anal dilators, enema tips, and thermometers. Among the former, a cursory check of the literature during the past several years reveals a bizarre group, ranging from vegetables, such as cucumbers and onions, to such solid objects as flashlights, light bulbs, spectacles, and even an umbrella handle![4] By far the commonest objects introduced were made of glass, and these ranged from glass tumblers to various types of bottles.[1-9]

In general the objects introduced by impalement are either introduced maliciously, usually during a drinking bout as a practical joke, or self-inserted for autoerotic gratification, which apparently results from pressure over the prostate and seminal vesicles. Occasionally the objects may be introduced for such reasons as constipation, itching piles, etc.

Many methods of treatment have been advised, and no standard treatment is applicable to all cases. When perforation of the sigmoid is suspected, laparotomy should not be delayed.

The following case is presented in the hope that it may prove helpful in the treatment of some of these patients.

Report of Case

A 45-year-old white man entered the Veterans' Administration Center at Whipple, Ariz. on June 2, 1957, complaining of obstipation of five days' duration. Further questioning revealed that the patient had been intoxicated for three days before his constipation. When he awoke he noted that his anal region was tender, and later on he felt a hard object in the left lower quadrant of his abdomen and decided that "something was wrong". He was seen by the O. D., who ordered an abdominal x-ray. This was reported as showing a glass bottle, measuring 23×7 cm., in the rectosigmoid, with the neck of the bottle directed superiorly and toward the left. The lower portion of the bottle was at the level of the symphysis pubis.

The patient was not in any acute distress and was given sedatives and put to bed. He was seen by me on the following morning. Examination disclosed a patient obviously suffering from acute embarrassment who answered questions just above a whisper. He denied self-insertion of the bottle or any past history of sexual perversion concerning the anal region. It was obvious that the patient had said all he was going to say. Palpation of the left lower abdomen revealed a hard object, clearly the neck of the bottle. On anal examination a profuse, foul-smelling mucous discharge was noted. The anus was markedly dilated, and on rectal examination the base of a bottle was felt impinged under the sacrum.

The patient was given 1 gm. of neomycin sulfate by mouth and prepared for operation. It was suggested by our anesthetist, Dr. H. E. White, that a tonsil snare threaded with a soft No. 14 rubber catheter would be a good instrument with which to grasp the bottle. The patient was given a spinal anesthetic and placed in the prone jackknife position on the operating table, but not until an assistant had placed his hand over the left lower portion of the patient's abdomen to grasp and control the neck of the bottle in order to prevent upward migration. The anus was then dilated and held open with several Sims retractors, and the base of the bottle was clearly in view. The rubber-covered wire of the tonsil snare was then threaded around the base of the bottle, using both fingers and a long thumb forceps, for a distance of about one inch. The snare was then tightened firmly,

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Chief, Surgical Service, Veterans' Administration Center.

Fig. 1.—Roentgenogram showing a glass bottle which was inserted into the patient's rectum during a drinking bout.

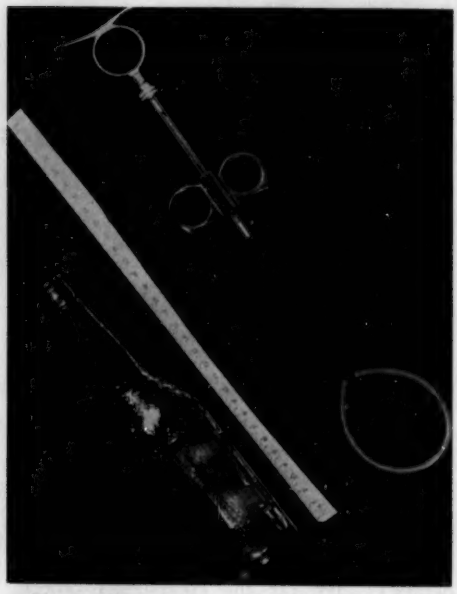

Fig. 2.—Glass bottle removed from the patient's rectosigmoid region, and the tonsil snare, with rubber-covered wire, used to remove the bottle.

and pressure was exerted downward through the abdomen on the neck of the bottle toward the rectum by an assistant while traction was exerted from below through the tonsil snare. The sum of the two forces was through the axis of the bottle, thereby giving a steady even force, and the bottle was easily delivered. The left index finger was swept around the base of the bottle over the mucosa during delivery to facilitate removal. The bottle measured 20 cm. in length and 6 cm. in diameter at the base, and there was a short piece of cord attached to the neck.

Upon completion of the removal a proctoscopic study was done with ease to the 25-cm. level. No perforations were noted, but considerable edema of the rectosigmoid was noted.

The patient's postoperative course was uneventful. The neomycin was continued for two days; other than that his treatment was symptomatic. A rectal examination on the seventh postoperative day revealed fairly good tone with only minimal tenderness. The patient was anxious to leave the hospital and was discharged on the eighth postoperative day.

Summary

1. A brief discussion of the impalement type of foreign bodies introduced through the anus is given.

2. A case of a bottle in the rectosigmoid is presented, with illustrations.

3. A method of removing a bottle from the rectosigmoid using a tonsil snare is described.

P. O. Box 61.

REFERENCES

1. Bacon, H. E.: Anus, Rectum, Sigmoid Colon: Diagnosis and Treatment, Ed. 3, Philadelphia, J. B. Lippincott Company, 1949, pp. 919-922.

2. Gerendasy, J.: Foreign Body in the Rectum, Am. J. Surg. 91:126-129 (Jan.) 1956.

3. Hunter, R. C., Jr.: Foreign Body (Light Bulb) in Recto-Sigmoid, U. S. Armed Forces M. J. 5:1058-1060 (July) 1954.

4. Kleitsch, W. P.: Foreign Bodies in the Rectum, Mil. Surgeon 105:215-217 (Sept.) 1949.

5. Marks, I. N.: Foreign Bodies in Rectum: An Unusual Collection, South African M. J. 25: 730-731 (Oct.) 1951.

6. Panasci, E. H., and Zutranen, H. A.: A Cucumber Perforating Rectosigmoid Junction, Am. J. Proct. 7:230-232 (June) 1956.

7. ReBell, F. G.: Problem of Foreign Bodies in the Colon and Rectum, Am. J. Surg. 76:678-686 (Dec.) 1948.

8. Ryan, J. E.: Proctologic Oddities, South. M. J. 47:771-773 (Aug.) 1954.

9. Scomahorn, M. O.: Unusual Foreign Body in the Rectum, Am. J. Proct. 7:499-502 (Dec.) 1956.

Angular Dermoids

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A recently encountered patient has again brought to our attention the entity of angular dermoids of the eyebrow. We wish to relate our experiences with these tumors. The variability in location of dermoid tumors is well known. Dermoids of the eyebrow are usually categorized with orbital tumors and are frequently dealt with by the ophthalmologist.

An angular dermoid occurs at the outer angle of the eye, beneath or in close proximity to the eyebrow (Fig. 1). It contains elements derived from two germ layers: mesoderm and ectoderm. Developmentally, these tumors are thought to represent inclusions of ectoderm along the lines of closing fissures; however, this concept cannot be completely accepted, since facial fissures close by subepithelial extension only. These tumors may be closely related to an anomalous fusion of the visceral and paraxial tissues in the orbital area.[3]

Characteristically, these tumors are ovid, soft to firm, and may be lobulated, containing a lipomatous element as well as having a cystic character. Cystic dermoids contain hair, sweat glands, sebaceous material, and squamous epithelium (Fig. 2). Transillumination is poor to absent. They grow slowly and are commonly symptomless. The most frequent complaints are of (*a*) cosmetic and (*b*) pain. The pain is dull and constant. It is generally located over the hemicranium, particularly the temporal area, but may be retrobulbar. The pain is due to direct or reflex irritation of the zygomaticotemporal and supraorbital nerves.

These tumors are generally removed prior to attaining an unsightly size. Primary malignancy is quite rare. The finding of a squamous-cell carcinoma developing in the cyst wall of an intraorbital dermoid has been reported by Jones.[2]

Though dermoids are reported occurring throughout the orbital area, only those beneath the eyebrow can be "snap-diagnosed."[1] Ward and Hendrick include in the differential diagnosis dermatofibroma, dermatolipoma, and neurofibroma.[5] Metastases and encephaloceles do not occur in this location. It should always be remembered that a dermoid in this location may be connected by a tiny stalk to a parent, intraocular dermoid.[4] Skull films and ophthalmologic and neurologic examinations are generally negative and reveal only incidental findings. Rarely, temporal hyperesthesia may be present.

The treatment is surgical excision, and the cure is complete. Six of these tumors have been removed under general anesthesia, and

Fig. 1.—Patient, demonstrating the site of an angular dermoid.

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From the Department of Surgery of the Bowman Gray School of Medicine of Wake Forest College.

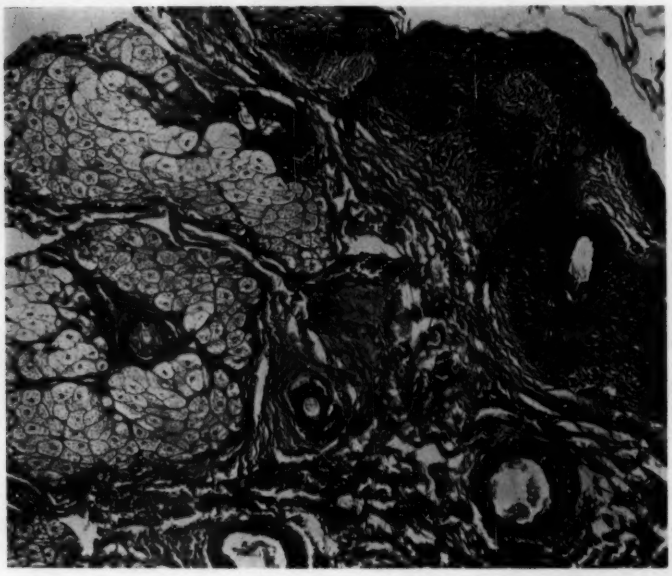

Fig. 2.—Photomicrograph of the cyst wall, demonstrating the typical findings of stratified squamous epithelium, dense connective tissue, sebaceous glands, and hair follicles. A lipomatous element is missing from this tumor.

in one additional case surgery was performed under local anesthesia with an anesthetist at hand for general anesthesia. After an initial experience in which local anesthesia was inadequate, the wound was closed and excision was performed the next day under general anesthesia.

Angular dermoids may be ensheathed by extensive meshes of filaments from the zygomaticotemporal nerve. The temporal fascia may enclose them. The superficial temporal, the transverse facial, and the supraorbital arteries are in immediate proximity to the tumor and can be ligated with impunity. The primary blood supply to the tumor is from the zygomatic branch of the lacrimal artery. Division of the fascial and neural filaments results in negligible, permanent hypesthesia. Drains have not been necessary. Plastic dermal closures with intracuticular absorbable surgical (gut) sutures or dermal 00000 nylon have given excellent cosmetic results.

Summary

Angular dermoids may be encountered by the general surgeon. Their diagnosis is easily made. The treatment is surgical removal. They may represent extensions from an intraocular dermoid. Because of difficulty in establishing adequate local anesthesia, the surgeon should be prepared to supplement local with general anesthesia during the operative procedure.

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REFERENCES

1. Bailey, H.: Demonstrations of Physical Signs in Clinical Surgery, Ed. 11, Baltimore, the Williams & Wilkins Company, 1949, p. 41.

2. Jones, A. C.: Oil Cyst of the Orbit with Carcinomatosis, Am. J. Ophth. 18:532-535 (June) 1935.

3. Mann, I.: Developmental Abnormalities of the Eye, London, Cambridge University Press, 1937, pp. 411-412.

4. Palomar, C. F.: Quiste dermoide orbitotemporal, Rev. med. Barcelona 9:99-103, 1928; cited by Samuels, B.: Tr. Am. Ophth. Soc. 34:226, 1936.

5. Ward, G. E., and Hendrick, J. W.: Diagnosis and Treatment of Tumors of the Head and Neck (Not Including the Central Nervous System), Baltimore, the Williams & Wilkins Company, 1950, pp. 495 and 551.

Radical Mastectomy for Carcinoma of the Breast During Pregnancy

Report of a Case with a Fifteen-Year Follow-Up

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Over a period of years, there has been considerable variation in opinion concerning the advisability of surgical therapy for cancer of the breast occurring during pregnancy. Since the occurrence of breast cancer during pregnancy is uncommon, it seems desirable at this time to make available the report on a patient who, 15 years after a radical mastectomy was performed during pregnancy, is still alive and doing well. It is of interest to note that there has been only one other case reported in the literature with the same survival span.[2]

In 1937, Harrington[6] reported a 13.2% survival for five years in a group of 99 women who had had an operation for carcinoma of the breast during pregnancy.

Haagensen and Stout[4] published a report in 1943 in which they concluded that a radical mastectomy during pregnancy was unjustifiable in cases of carcinoma of the breast. By 1951, when Haagensen and his group[5] published a further report, they had still not encountered a "curable" case. However, in 1949, Brooks and Proffitt[2] had come out with a more encouraging report. This involved a 33-year-old woman who noted a hard lump in her breast when she was in her eighth month of pregnancy. Four months later, she had a radical mastectomy for adenocarcinoma with axillary metastases. Fifteen and a half years later, this patient was still alive and well.

More recently, Ackerman[1] reported two cases in which a radical mastectomy had been done during pregnancy or lactation, and, although no cure had been effected in either of these patients, one survived for 10 years after the operation.

Of particular interest is the report that Cheek[3] issued on the survey he had made of 47 authorities with special interest in carcinoma of the breast. He assembled from among them reports of 151 patients in whom pregnancy was associated with carcinoma of the breast, and found that in this entire group there were eight five-year cures, making a rate of 5.3%.

Among the surgeons he surveyed, opinion was divided on the question of terminating the pregnancy. Of 35 who responded to the questionnaire, 10 thought there was no reason to terminate the pregnancy; 19 replied that it should be terminated in the first trimester, and, of these, 16 felt that pregnancy should be terminated in the second, as well as in the first, trimester. Eleven of the nineteen were of the opinion that discovery of carcinoma in the breast at any time during pregnancy constituted a definite indication for interruption of the pregnancy.

In 1956, White and White[7] reported that, in reviewing 3245 patients with breast cancer, they found 2% to be pregnant at the time the cancer was discovered. They further reported that those treated promptly, that is, while the disease was still localized in the breast, did very well, but that the patients in whom metastasis had occurred were far less fortunate.

The case reported here represents still another opinion on the question of terminating pregnancy or performing radical surgery in a patient with carcinoma of the breast.

Submitted for publication Sept. 19, 1957.

From the Division of Surgery, the Roosevelt Hospital.

Report of Case

The patient, 29 years of age, was examined in July, 1937. Two tumors were found in her right breast, one in the upper outer quadrant and the other just above the areola, each measuring 1 cm. in diameter.

In January, 1938, she was admitted to the Roosevelt Hospital for an operation. I removed both these lumps and found them to be areas of chronic cystic mastitis. Three and a half years later, the patient was again examined in anticipation of a third pregnancy, and both breasts were found to be normal. (Her two children were 5 and 2 years old, and both had been delivered by Cesarian section.) About 18 months thereafter (February, 1942), when the patient was in her fifth month of pregnancy, it was found that she had a mass, 2.5 cm. in diameter, in the lower inner quadrant of the right breast, as well as one palpable gland in the axilla.

I performed a right radical mastectomy at the Roosevelt Hospital, and a pathological diagnosis was made of adenocarcinoma of the breast, Grade 3, in a lactating mammary gland. The lymph nodes that were examined were found free of disease.

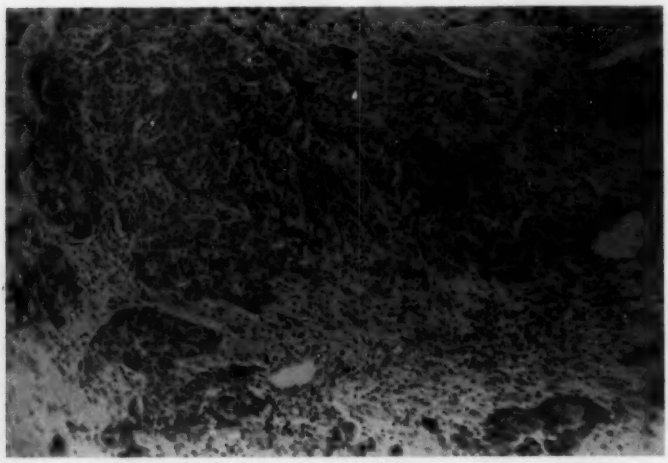
Three months later, in May, 1942, a Cesarian section was done, without removal of the ovaries. In July, 1957, the last time the patient was seen, she was still alive and free of any discoverable carcinoma.

Comment and Conclusion

Cancer of the breast is more virulent when it occurs during pregnancy than at any other time in a woman's life. This is probably due to the increased blood supply to the breasts during pregnancy and the possibility of stimulation of the cancer cells by the hormonal changes brought on by pregnancy.

Because of the enlargement of the breasts resulting from pregnancy, a cancerous swelling may not be detected, either by the patient or by her obstetrician, until the disease process has become well advanced. However, patients who become pregnant after previous trouble with their breasts do tend to be more alert to signs of change and to seek medical attention sooner. In these patients, the chances of earlier detection and longer survival will therefore be greater than in others.

The case reported here belongs to this group of patients, and the fact that the patient is well 15 years after surgical treatment, despite an intervening pregnancy, is consistent with the claim made here and in other reports that favorable outcome in such cases is well within the realm of possibility. Even the few cases that have been reported with long-term survival suggest that no woman with cancer of the breast during pregnancy should be denied the chance for cure that might be effected through radical mastectomy.



Photomicrograph of a section of the breast removed in February, 1942.

Mrs. Rose M. Schweitzer, editor of *Clinical Research,* Roosevelt Hospital, gave editorial assistance in the preparation of this paper.

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REFERENCES

1. Ackerman, L. V.: Evaluation of Treatment of Cancer of Breast at University of Edinburgh, Cancer 8:883, 1955.

2. Brooks, B., and Proffitt, J. N.: Influence of Pregnancy on Cancer of the Breast, Surgery 25:1, 1949.

3. Cheek, J. H.: Survey of Current Opinions Concerning Carcinoma of the Breast Occurring During Pregnancy, A. M. A. Arch. Surg. 66: 664, 1953.

4. Haagensen, C. D., and Stout, A. P.: Carcinoma of the Breast: Criteria of Operability, Ann. Surg. 118:859, 1943.

5. Haagensen, C. D., and Stout, A. P.: Carcinoma of the Breast: Results of Treatment, Ann. Surg. 134:151, 1951.

6. Harrington, S. W.: Carcinoma of the Breast: Results of Surgical Treatment When the Carcinoma Occurred in the Course of Pregnancy or Lactation and When Pregnancy Occurred Subsequent to Operation, Ann. Surg. 106:690, 1937.

7. White, T. T., and White, W. C.: Breast Cancer and Pregnancy: Report of 49 Cases Followed 5 Years, Ann. Surg. 144:384, 1956.

Carcinoma in Chronic Ulcerative Colitis

Report of a Case, with Death in Six Weeks

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A case of chronic ulcerative colitis is reported in which a carcinoma developed 17 years after onset of the disease. The patient was treated with a radical subtotal colectomy and ileostomy. The pathological report confirmed the presence of a 3 cm., well-differentiated carcinoma of the right transverse colon with 59 negative lymph nodes. The patient died six weeks following operation with widespread metastatic disease, confirmed at autopsy.

The purpose in again discussing neoplasia in chronic ulcerative colitis is to reiterate the virulence of the cancer, even in the presence of negative lymph nodes; to point out the gravity of shedding viable cancer cells, especially in the presence of a nourishing incubating medium, such as ascitic fluid, and to discuss the remarkable capacity for malignant-cell transplantation of a patient with ulcerative colitis without a spleen.

Report of Case

A 32-year-old itinerant waiter who had a history of ulcerative colitis for 17 years presented himself in the accident room of the Lynn Hospital complaining of the abrupt onset of periumbilical and hypogastric cramps, of 24 hours' duration. He also complained of constipation without melena. There was no history of anorexia or weight loss. Seventeen years previously, he had been advised to have a colectomy and ileostomy at the Massachusetts General Hospital for ulcerative colitis, with which he had 15-20 bowel movements per day. The operation had been refused. After four years of intractable diarrhea, the disease had gone into spontaneous remission, and he was free of symptoms until seven years later, when he had a flare-up of the disease. Following that hospitalization, the ulcerative colitis underwent a second spontaneous remission which lasted until the present episode, in the summer of 1956.

The past history was pertinent in that he had been treated for infectious hepatitis at the Boston City Hospital in 1950. He was advised to restrict the use of alcohol, but he had elected to become a moderately heavy drinker during the past five years.

Physical examination revealed an afebrile, dehydrated, well-developed, well-nourished 32-year-old white man. The pertinent findings were limited to the abdomen. The abdomen was slightly distended and tender along the entire course of the colon. Peristalsis was hyperactive but normal-pitched. No masses were palpable other than the liver, which extended 2 cm. below the right costal margin. Rectal examination revealed no masses or tenderness, but the stool was guaiac-postive. A flat film of the abdomen was negative. The white blood cell count was 12,900 per cubic millimeter.

This episode was interpreted as a recrudescence of chronic, remitting ulcerative colitis. He was placed on strict bed rest and a regimen of nothing by mouth, intravenous fluids, mild sedation, and phthalylsulfathiazole U. S. P. (Sulfathalidine). The following day he felt improved, with complete disappearance of his tenderness. He improved, steadily and on the fourth day a sigmoidoscopy was done, revealing an edematous, nonulcerated mucosa, which bled easily when wiped. The rectal lumen was easily distensible. On the sixth day after admission a barium enema study was carried out, demonstrating a constricted area with shelf-like margins in the right transverse colon, in addition to changes consistent with long-standing ulcerative colitis. The defect in the transverse colon was persistent in a repeat barium enema.

The following preoperative laboratory studies were obtained: nonprotein nitrogen 23 mg., blood sugar 103 mg., per 100 cc.; chlorides 103 mEq/L., sodium 143 mEq/L., and potassium 3.5 mEq/L.;

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hemoglobin 13.9 gm. per 100 cc.; white cells 9200 per cubic millimeter; prothrombin time 100%; total protein 6.4 gm., albumin 4.1 gm., and globulin 2.3 gm., per 100 cc. Urinalysis negative.

At the time of operation the peritoneal cavity contained about 500 cc. of straw-colored fluid. The liver appeared slightly enlarged, with evidence of scarring. The peritoneal surfaces were smooth and glistening. In addition to the picture of typical ulcerative colitis, a small, button-like carcinoma was present in the right transverse colon. There was no gross evidence of metastatic spread. The right and left peritoneal attachments were incised, and the greater omentum and as much mesentery as possible were excised. In attempting to free a high splenic flexure, the splenic capsule was torn, making it mandatory to sacrifice this organ. An ileostomy was made in the right lower quadrant. The rectum was not resected. The patient tolerated the operation fairly well in spite of considerable blood loss.

Pathological Report.—The specimen consisted of terminal ileum and colon, measuring 125 cm. in length. The large bowel displayed thickening and multiple shallow but confluent ulcerations, the area of involvement extending from the cecum to the descending colon. There was a firm, ulcerated, 3 cm. lesion in the right transverse colon. Fifty-nine lymph nodes were dissected from the specimen. The final diagnosis was chronic ulcerative colitis; adenocarcinoma of the transverse colon, well differentiated, with full-thickness invasion of the bowel wall, and reactive hyperplasia of lymph nodes.

Clinical Course.—His initial postoperative course was very smooth. The ileostomy worked well from the first postoperative day. However, by the fifth day the abdomen had become very distended. The clinical impression of fluid was confirmed by paracentesis, which yielded 5000 cc. of slightly blood-tinged fluid. Cell block for malignant cells was negative. The ascites was interpreted as the result of overload of a poorly compensated liver from radical disruption of the collateral blood channels or a propagating thrombosis of the splenic vein into the portal vein. Sulfobromophthalein (BSP) retention determined on the eighth postoperative day was 9.5% in 45 minutes. He was placed on a low-salt regimen, high-carbohydrate intake, and diuretics, without clinical improvement. In spite of all conservative supportive measures, his course was steadily downhill. He became jaundiced five weeks postoperatively. Laboratory tests revealed both hepatocellular and obstructive icterus. During the sixth week he began to bleed massively from the gastrointestinal tract. The hemorrhage failed to respond to any treatment, and he succumbed six weeks following radical subtotal colectomy and ileostomy.

Autopsy Report.—Postmortem examination revealed carcinomatosis of the entire abdominal cavity. The liver was studded with carcinoma, and the common duct was partially obstructed by a large retroperitoneal tumor mass. The small bowel was glued together by neoplastic adhesions. The peritoneal surface was seeded with implants of cancer, and tumor was discovered growing into the healed abdominal wound. There was also metastatic disease in the lungs. The portal vein was completely surrounded by tumor and was partially occluded by an organizing thrombus. The splenic vein was obliterated by thrombus.

Comment

Obviously, this case points up the virulence of cancer in younger adults, particularly in those with long-standing, remitting ulcerative colitis. The poor prognosis is well known. Wechesser and Chinn [1] reported an incidence of 3.4% of cancer in 118 cases of chronic ulcerative colitis studied at the University Hospitals of Cleveland. Their longest survival was 17 months. However, Wheelock and Warren [2] discovered an incidence of 8.8% in 319 cases at the Massachusetts General Hospital, but they thought it might have been higher had all the cases been traceable. Of the 31 patients, 7 were alive in 1955 and 2 survived for five or more years.

Bargen et al.[3] pointed out that cancer occurred in patients with ulcerative colitis on an average of 30 times as frequently as in persons of the general population of similar age groups. Dennis and Karlson [4] concluded, from a statistical survey of their patients with chronic ulcerative colitis, that each patient leaving his colon in place runs about a 1.6% risk of developing cancer in that colon for each year over nine years in which he retains it.

Counsell and Dukes,[5] in a histological study of cancer developing in chronic ulcerative colitis, observed that the tumor was often anaplastic, with extreme invasive and metastatic tendencies. They noted very early lymphatic spread.

The present case seems important from three other aspects: First, extensive carcinomatosis was seen at autopsy; yet negative lymph nodes and no gross evidence of

spread was found at operation. The pathological report revealed a well-differentiated cancer, which was growing through all layers of the bowel wall. The invasive nature of the tumor made it possible for viable cancer cells to be shed into the free peritoneal cavity into a nourishing medium of ascites fluid. Second, because of technical necessity, the spleen was ablated. The immune factors as related to the spleen are not well known. The "something" that was done to lower the host's resistance to tumor-cell transplantability may have been related to the excision of the spleen. Meigs [6] noted that in certain cases of carcinoma of the cervix there was a large spleen and thought that it may have reflected a favorable response to the cancer. Third, the operation may have played a role in producing carcinomatosis in this case. This is extremely difficult to interpret. Crile [7] believes that tissue damage directly influences spread of cancer in serosal cavities. He maintains that even low-grade cancer when cut across can seed itself. From cytological studies, he noted the constant exfoliation of cells from exposed cancer and observed that these cells survived more easily in the presence of antibiotics.

Finally, every effort should be made to follow patients with ulcerative colitis with adequate x-ray studies and sigmoidoscopies. Rectal washings for evaluation of malignant cells may prove helpful. If there is good clinical reason to suspect malignant degeneration in long-standing cases of ulcerative colitis, even though a cancer is not demonstrable by x-ray or sigmoidoscopy, colectomy and ileostomy are indicated.

Summary and Conclusions

The case is reported of a 32-year-old man with a 17-year history of chronic ulcerative colitis who developed a 3 cm. carcinoma of the colon with negative nodes, who was treated by radical subtotal cholectomy and ileostomy, and who died of carcinomatosis six weeks after operation.

The incidence, prognosis, invasive character, and metastatic tendency of carcinoma in cases of long-standing ulcerative colitis are reviewed.

All cases of ulcerative colitis should have liver function tests prior to operation, because of the increased incidence of cirrhosis in long-standing ulcerative colitis.

Every effort should be made at operation to protect surrounding organs and serosal cavities from exfoliating cells of exposed cancer.

The unusual viability of the cancer in this case may have been due to the loss of immune factors produced by the spleen and/or to the tissue injury at the time of operation plus antibiotic coverage.

The immune factors of the spleen and the effect of operation on neoplasia need further clarification.

Cytological studies of rectal washings may be helpfully employed in cases of questionable malignant degeneration of the colon.

If there are good clinical grounds for suspecting cancer in cases of long-standing ulcerative colitis, even in the face of negative x-rays and sigmoidoscopy, colectomy and ileostomy are indicated.

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REFERENCES

1. Wechesser, E. C., and Chinn, A. B.: Carcinoma of Colon Complicating Ulcerative Colitis, J. A. M. A. 152:905-908 (July) 1953.

2. Wheelock, F. C., Jr., and Warren, R.: Ulcerative Colitis: Follow-Up Studies, New England J. Med. 252:421-425 (March 17) 1955.

3. Bargen, J. A.; Sauer, W. G.; Sloan, W. P., and Gage, R. P.: Development of Cancer in Chronic Ulcerative Colitis, Gastroenterology 26: 32-37 (Jan.) 1954.

4. Dennis, C., and Karlson, K. E.: Surgical Measures as Supplements to the Management of Idiopathic Ulcerative Colitis, Surgery 32:892-912 (Nov.) 1952.

5. Counsell, P. B., and Dukes, C. E.: Association of Chronic Ulcerative Colitis and Cancer of the Rectum and Colon, Brit. J. Surg. 39:485-495 (May) 1952.

6. Meigs, J. V.: Surgical Treatment of Carcinoma of the Cervix, New York, Grune & Stratton, Inc., 1954, pp. 155-156.

7. Crile, G.: Factors Influencing the Spread of Cancer, Surg. Gynec. & Obst. 103:342-352 (Sept.) 1956.

Correspondence

IN VITRO OXYGENATION OF FRESH WHOLE BLOOD FOR ARTERIAL PERFUSION

To the Editor:—In the August, 1957, issue of this journal there appeared an article by Button, Bernhard, and Walter entitled "In Vitro Oxygenation of Fresh Whole Blood for Arterial Perfusion."

These authors describe a simple closed method utilizing ion-exchange resin columns and plastic bags for the collection and in vitro oxygenation of fresh whole blood for arterial perfusion. They propose this as a simple system for arterial perfusion of the circulation during repair of congenital defects of the right heart in children weighing up to 15 kg. and for perfusing the coronary and cerebral afferent vessels as an adjunct in cardiac surgery under hypothermia. The authors cite no results using this system as proposed in either experimental or clinical cardiac operations.

When the donor's blood passes through the ion-exchange resin column, it is rendered incoagulable through removal of its divalent cations, the most important of which is calcium. According to their proposal, this calcium-free oxygenated blood would be perfused via the arterial system into the coronary circulation.

Since the work of Ringer (*J. Physiol.* 4:29, 1883), it has been recognized that calcium is one of the essential cations for the maintenance of normal cardiac rhythm. Recent experiments by Cookson et al. (*Ann. Surg.* 139:430, 1954) showed that arterial perfusion with oxygenated blood in which the calcium was bound un-ionized by citrate resulted in poor cardiac output in normothermic dogs, and ventricular fibrillation or cardiac arrest in hypothermic dogs. Unpublished animal experiments in our laboratory in which the arterial system was perfused with decalcified whole blood (drawn by the same ion-exchange method and equipment as that described by Button, Bernhard, and Walter) have resulted in serious electrocardiographic changes, leading to weakened myocardial contractions, ventricular fibrillation, or arrest.

For the past two years we have been interested in the development of methods and equipment which might simplify the collection and processing of donor blood for cardiac operations. One of our methods, still under study, employs the use of resin-decalcified whole blood to which a preservative is added at the time of the blood donation. However, in our procedure, when this blood is removed from storage and used for arterial perfusion, it is then heparinized, after which the ionized calcium and magnesium concentrations are restored to normal just before use. Work with this latter method is still in progress, and recommendation of its use must await extensive in vivo experiments before the complete safety of such blood could be assured.

In the meantime, those tempted to employ Button, Bernhard, and Walter's method as a simple means of circumventing proved present-day pump oxygenators for the small cardiac patient or for supplementing the hypothermic heart should be warned of the ill effects of perfusing the heart with decalcified blood.

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POSSIBLE ETIOLOGY OF AINHUM

To the Editor:—The article entitled "Ainhum (Dactylosis Spontanea)" by W. L. Norton, A. M. Sala, and M. E. Silverstein, in the September, 1957, issue of the Archives, has attracted my special attention because of a pertinent incident in my naval experience which may sufficiently engage your interest to merit publication.

In 1945, while serving as Chief of Surgery at the U. S. Naval Hospital, No. 203, in Guam, Marianna Islands, a man in his middle 60's was admitted to my service with an unrelated condition. He had, as an incidental finding, what appeared to be a typical example

of well-advanced ainhum, involving his fourth right toe. He offered no complaint with respect to it. I "recognized" it at once, and, aware of its unusual nature, I demonstrated the case to a number of colleagues from a nearby NAMRU (Naval Medical Research Unit). These included a prominent dermatologist and consultants equally distinguished in the fields of pathology, tropical medicine, and surgery. All agreed that this was indeed a case of ainhum and were appropriately elated over having observed an example of this rare and fascinating lesion.

After the consultants had left the hospital, one of my native Chamorro nurses approached me somewhat diffidently, saying: "Doctor, I didn't understand all that was said about this man, but I think I know what is the matter with his toe." These nurses, products of the Naval Hospital before the Japanese occupation of Guam, were exceptionally well trained, by any standard, and I always listened respectfully to their comments.

The nurse explained that there was a traditional native method, based, of course, on empirical observation, and probably centuries old, for treating infections of "expendable" digits. They knew, she said, that when a toe or finger became badly infected, a severe painful swelling of the groin or axilla frequently followed and that the victim often succumbed to it. They had found that if a piece of grass or string were snugly bound around the base of the part, the swelling would be prevented and the patient would recover, though he often lost the digit if the constriction were not removed in time. She said this risk was readily accepted if the digit was relatively nonessential, such as a fourth or fifth toe, but there would be greater reluctance in the case of a finger or the great toe.

She went on to say that when a native had been employing folk medical methods he was embarrassed to admit it when consulting a trained physician, fearing ridicule, but she believed that this patient would tell me about it if she promised him I would not laugh at him.

Needless to say, the nurse's diagnosis was correct, and the patient readily admitted it. He had gotten a splinter in his toe, which he had been unable to extract, and when it began to fester, he had bound the base with a piece of grass, effectively preventing the swelling of his groin, and he regarded the loss of the toe, now well mummified, with a typical "pseudo-fibrous" constriction at its base, as inconsequential. He had, of course, removed the grass before he came to the hospital.

The implication is obvious, and, in reviewing the account in the article which has prompted this letter, several points seem worth noting.

The condition is largely confined to tropical countries or people, where the incidence of trauma and infection of the pedal digits is likely to be high, and where traditional folk methods of self-treatment are likely to have developed. It usually affects the less essential toes and is unusual in the fingers. At least one British authority, cited by the authors, regards trauma as a factor, and Grschebin is quoted as believing that no single etiological factor, whatever it may be, can be regarded as common to all cases.

It seems reasonable to conjecture that at least a significant proportion of supposed cases of ainhum are actually the result of a factitious mechanism such as this and do not really represent true spontaneous amputation. Indeed, it is conceivable that with careful and tactful questioning this simple and logical explanation may be found to obtain in most cases of ainhum.

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Surgery Illustrated

Some Complications of Circumcision and Their Surgical Repair

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Complications of circumcision have most commonly consisted of bleeding and infection, the latter usually mild.[1,2] However, serious and even fatal infections have occurred as a result of both ritual and medical circumcision. Diphtheritic infection of the wound,[3] fatal staphylococcal bronchopneumonia,[4] staphylococcal septicemia resulting in osteomyelitis of the femur,[5] and tetanus[6] have been reported. Of more immediate interest to the physician, be he general practitioner, plastic surgeon, urologist, obstetrician, or general surgeon, are the complications of circumcision resulting in deformity or dysfunction of the penis itself. It is the purpose of this paper to report several complications of circumcision requiring surgical repair.

Submitted for publication May 13, 1957.

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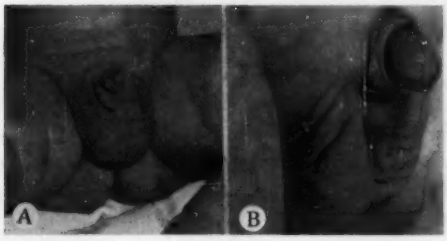
The opinions or assertions contained herein are the private ones of the writers and are not to be construed as official or reflecting the views of the Navy Department or the Naval Service at large.

Fig. 1.—*A*, "concealed penis." The penis was forced into a completely subcutaneous position by wound contraction following circumcision. Prominence which is visible is site of a small fistula leading to the urethral meatus, deep to the level of pubic skin.

B, result six weeks after liberation of penis. Elevation of tissue seen in *A* is now located at the base of the scrotum, below the penis. Addition of skin to shaft will be required at a later operation.

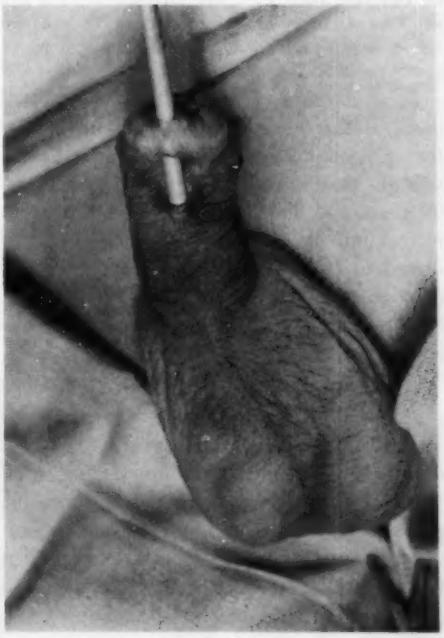


Concealed Penis

A 2-month-old male infant was admitted to St. Louis Children's Hospital because of penile deformity and difficulty in urination.

The history indicated that the infant at birth was a normal, full-term child except that the penis seemed shorter than normal. Circumcision was carried out with the use of a Gomco clamp. In a

Fig. 2.—Large urethral fistula. A catheter traverses the extensive defect. The accompanying chordee, due to scar contracture, is not apparent from this view. A two-stage repair is under way, the first operation, for relief of ventral flexion, having been completed.



few weeks, however, the mother returned to the physician with the infant because she had noticed that "the skin had grown back over the penis," and the child had been experiencing difficulty in urination. This skin was reportedly excised but "grew over again," and the infant was referred for correction of this deformity.

Physical examination on admission revealed a healthy, normal male infant except for the external genitalia. The penis was not visible and was found to be completely buried in the subcutaneous tissue of the pubic region and scrotum. A sinus emerged through a small, scarred aperture in a tag of tissue just above the scrotum (Fig. 1*A*). The scrotum was normal and contained both testes. Palpation of the pubic area disclosed what appeared to be the shaft of a normal penis subcutaneously, but it was impossible to find and catheterize the urethral meatus.

A vertical incision was made in the pubic skin overlying the palpable penis, splitting the sinus tract. The glans penis was found enveloped in what proved to be the tightly adherent mucous membrane of the prepuce. This was dissected from the glans and retracted. Considerable smegma was found in the coronal sulcus. The shaft of the penis was normal. The free edge of mucous membrane was then sutured to the surrounding skin edges of the operative wound. At the conclusion of the operation the glans was in a normal external position, as illustrated in Figure 1*B*, but a skin deficiency remained. It was decided to postpone replacement of this skin until the child should reach the age of 3 or 4 years in order to conserve essential tissue and not risk an inadequate reconstructive operation in such a small infant at this time.

In attempting to reconstruct the development of this complication, it would appear that a combination of factors might be involved: Readherence of mucous membrane to glans and the tendency of the penis to retract into the fatty mons pubis may have united to force the penis into a submerged position. The circular circumcision wound then was free to contract to match-stem size and secure the organ in its trapped position.

Urethral Fistula

Urethral fistula as a sequela of circumcision is seemingly uncommon. Figure 2 is an operating-room photograph of the penis of a 10-year-old boy who was circumcised soon after birth. A complete segment of urethra was destroyed, resulting in a large defect of the urethra and chordee secondary to scar contracture. This situation, quite like that of congenital hypospadias with chordee, is being corrected by a two-stage repair, which has been described previously.[7] Two cases of subglandular urethral fistulas following circumcision have been treated, as illustrated in Figure 3*A*, *B*, and *C*. This is a simple and dependable technique which has proved valuable in the treatment of urethral fistulas associated with repair of hypospadias[8] (Fig. 4). Johnson reported a fistula of the penile urethra secondary to infection in the operative wound in an adult, with its repair by a method described by Davis.[9,10] A preliminary suprapubic cystotomy preceded the actual repair of the fistula.

Loss of Penile Skin

Loss of skin of the penis resulting from circumcision is not uncommon and presents no particular features different from those expected in loss of the skin of the penis following industrial and farm accidents. This loss has resulted from the removal of too much preputial skin,[1] the use of the high-frequency cutting current,[11] and local anesthetic agents or other injected substances mistaken for anesthetic solutions.[12] The application of partial-thickness skin grafts to the denuded shaft of the penis in such instances[12,13] has given excellent results (Figs. 5 and 6).

Laceration of Penis

Accidental circumcisional lacerations of the glans and urethral meatus have been encountered. An interesting case of partial amputation of the penis during circumcision, with its repair, has been reported by Lerner.[14]

Loss of Penis

Several cases of total or partial slough of the penis from use of the electrosurgical unit at circumcision have been reported to us by personal communication, and loss of the penis from the use of a rubber band as a tourniquet has been reported.[15] Figure

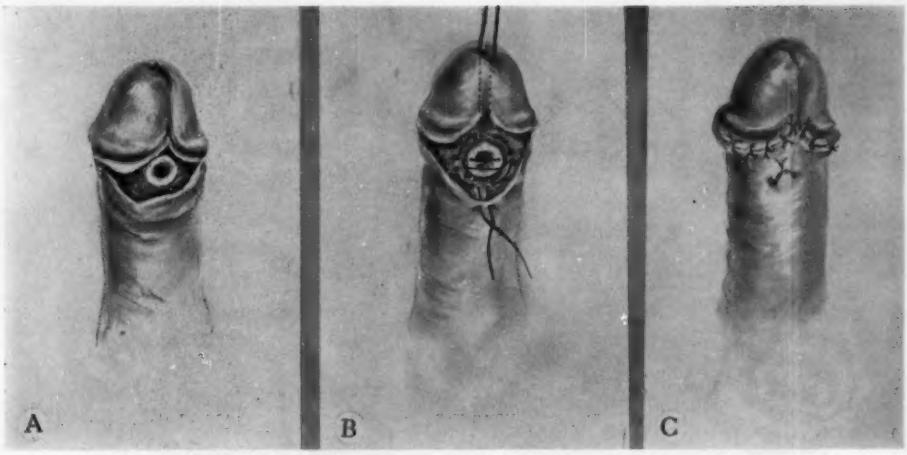
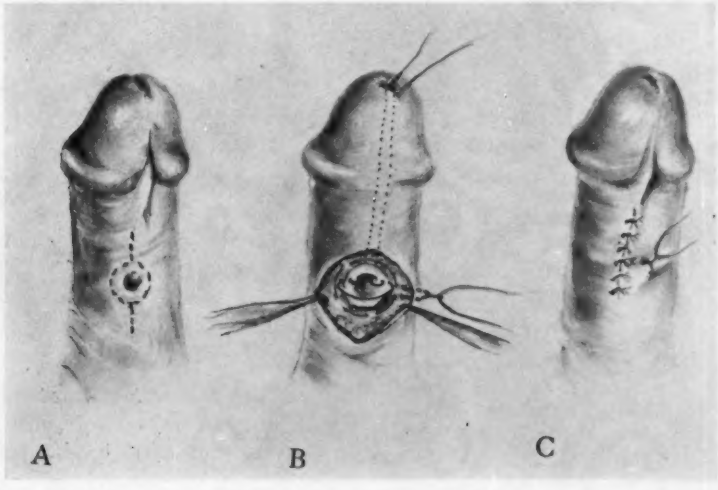


Fig. 3.—*A*, drawing of subglandular urethral fistula following circumcision. Skin of the undersurface of the penis has been mobilized by incision around the corona. More tissue can be gained by making a dorsal slit in the prepuce and bringing redundant tissue to the undersurface.

B, a purse-string suture has been placed around the mouth of the fistula. The ends of the purse-string suture have been brought through the flap of skin on the undersurface of the penis, where the suture will be tied so that the knot will be external rather than in the wound. The suture emerging from the meatus will ensure inversion of the mouth of the fistula when traction is exerted on it. After purse-string suture is tied, inverting stitch is removed through the meatus. No catheter is used, and the urinary stream is not diverted.

C, completion of operation, with fistula closed in watertight fashion by purse-string suture, which is tied on the outside of the skin to avoid unnecessary suture material within the wound. Redundant skin on the undersurface of the penis permits skin closure at a different level from that of the fistula. This overlapping of wound reduces likelihood of recurrence. The urinary stream is not diverted.

Fig. 4.—*A, B, C*, scheme illustrated in Figure 3 applied to urethral fistula in shaft of penis, such as might result from infection or hypospadias repair. The same principles are involved as those illustrated in Figure 3.



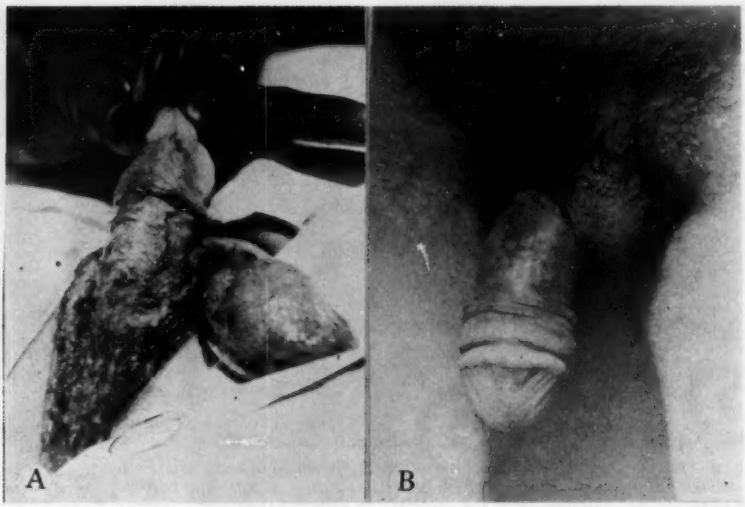
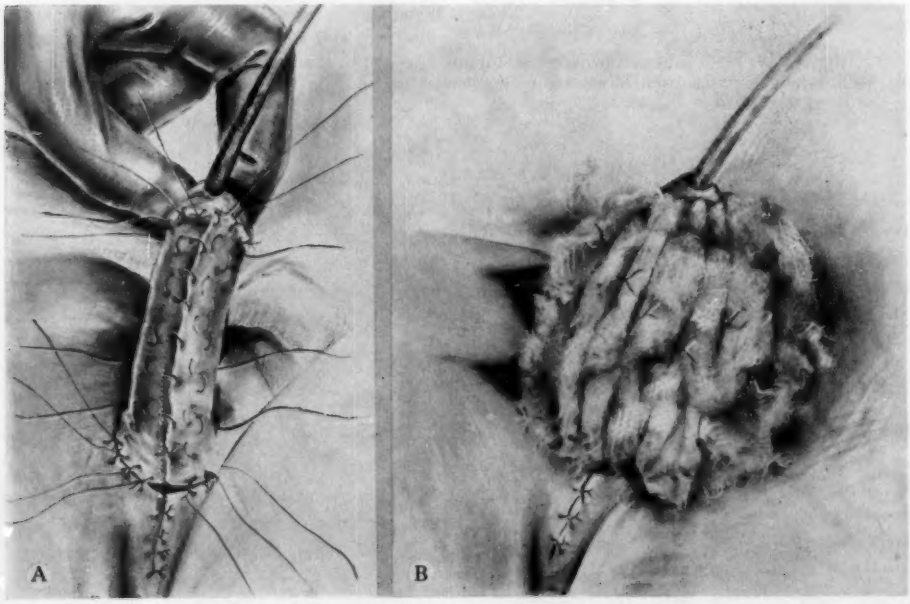


Fig. 5.—*A*, loss of scrotum, skin of shaft of penis, and one testis from trauma. Similar skin loss has been seen and repaired following circumcision.

B, result from immediate repair with free skin graft. This same procedure has been utilized to replace skin lost following injection of solution employed for local anesthesia during circumcision.

Fig. 6.—*A*, technique employed in patient shown in Figure 5*A* and *B*. Heavy split-thickness skin graft was sutured accurately to cover the skin defect. Sutures at glans and base of penis were left long and tied over cotton waste, as illustrated in *B*. This, along with additional circular dressings, splinted the wound and provided pressure. This technique has been employed in repair of skin loss following circumcision.



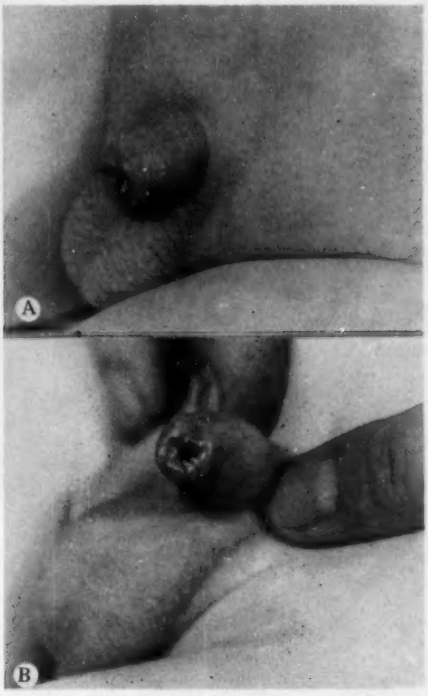


Fig. 7.—*A*, absence of glans following ritual circumcision. *B*, attempted retraction of penile skin, demonstrating fixation of skin to distal urethral stump.

7*A* and *B* are photographs of the penis of a 2½-year-old child who underwent ritual circumcision with loss of the entire glans. Urinary function is adequate at present.

Conclusions

1. Serious complications of circumcision appear to be unusual, but, considering the frequency of this operation, many disabling complications may occur which remain unreported.

2. While a simple operation, circumcision requires the same exactness of technique, attention to detail, and respect for tissues due any other surgical procedure.

3. Deforming or disabling complications of circumcision should be corrected at the earliest possible time and to an extent compatible with the age of the patient, with a normal-appearing and functioning penis as the goal.

Summary

1. An unusual complication of circumcision is reported and its initial correction described.

2. A technique for the repair of urethral fistulas resulting from circumcision or other causes is described.

3. The technique for resurfacing the penis with skin grafts is reviewed.

4. Additional reported complications of circumcision are cited.

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REFERENCES

1. Campbell, M.: Clinical Pediatric Urology, with section on Nephritis and Allied Diseases in Infancy and Childhood by E. Goettsch and J. D. Lyttle, Philadelphia, W. P. Saunders Company, 1951.

2. Pugh, W. S.: Circumcision, S. Clin. North America 15:461-470 (April) 1935.

3. Rosenstein, J. L.: Wound Diphtheria in the Newborn Infant Following Circumcision, J. Pediat. 18:657-685 (May) 1941.

4. Sauer, L. W.: Fatal Staphylococcal Bronchopneumonia Following Ritual Circumcision, Am. J. Obst. & Gynec. 46:583 (Oct.) 1943.

5. Altman, H.: Osteomyelitis of the Femur in an Infant, Bull. Hosp. Joint Dis. 7:109-113 (Oct.) 1946.

6. Gosden, M.: Tetanus Following Circumcision, Tr. Roy. Soc. Trop. Med. & Hyg. 28:645-648 (April) 1935.

7. Byars, L. T.: A Technique for Consistently Satisfactory Repair of Hypospadias, Surg. Gynec. & Obst. 100:184-190 (Feb.) 1955.

8. Byars, L. T.: Functional Restoration of Hypospadias Deformities, with Report of 60 Completed Cases, Surg. Gynec. & Obst. 92:149-154 (Feb.) 1951.

9. Johnson, S.: Persistent Urethral Fistula Following Circumcision, U. S. Nav. M. Bull. 49:120-122 (Jan.-Feb.) 1949.

10. Davis, D. M.: The Pedicle Tube-Graft in the Surgical Treatment of Hypospadias in the Male, with New Method of Closing Small Urethral Fistulas, Surg. Gynec. & Obst. 71:790-796 (Dec.) 1940.

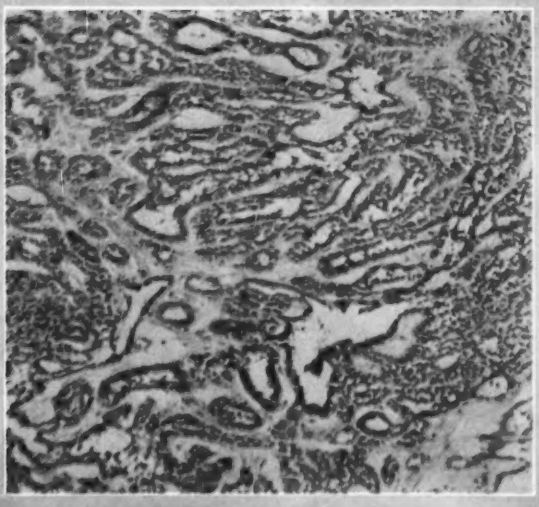
11. Hamm, W. G., and Kanthak, F. F.: Gangrene of the Penis Following Circumcision with High Frequency Current, South. M. J. 42:651-659 (Aug.) 1949.

12. Brown, J. B.: Restoration of the Entire Skin of the Penis, Surg. Gynec. & Obst. 65:362-365 (Sept.) 1937.

13. Byars, L. T.: Avulsion of Scrotum and Skin of Penis: Technique of Delayed and Immediate Repair, Surg. Gynec. & Obst. 77:326-329 (Sept.) 1943.

14. Lerner, B. L.: Amputation of the Penis as a Complication of Circumcision, M. Rec. & Ann. 46: 229-231 (Sept.) 1952.

15. Brimhall, J. B.: Gangrene Following Use of Rubber Band in Circumcision, St. Paul M. J., 4:490, 1902.



ADAMANTINOMA . . . 3 aspects

Radiograph *(upper left)* showing an adamantinoma in the lower end of a tibia in a man of 48 years. The lesion has caused lytic destruction and expansion of the contour of the affected part of the bone.

Photograph *(upper right)* of frontal section of specimen. The adamantinoma tumor tissue was clearly demarcated from the spongiosa. It was tough and firm but presented small areas of cystic degeneration.

Photomicrograph (x 90) *(left)* showing the alveolar glandular pattern so characteristic of certain fields of an adamantinoma.

Turn page for data on Osteogenic Sarcoma.

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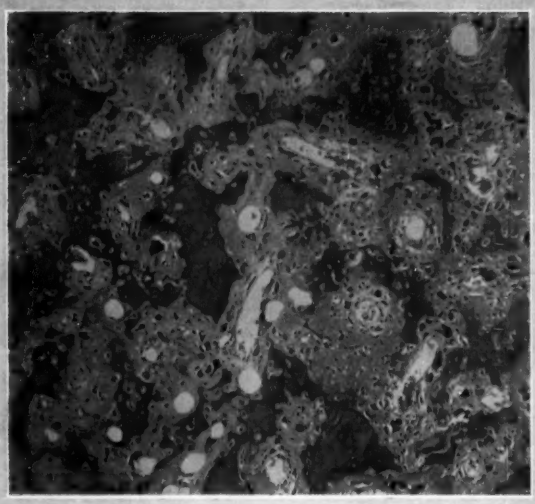
OSTEOGENIC SARCOMA . . . 3 aspects

Radiograph *(upper left)* of a highly ossifying osteogenic sarcoma in the upper part of the shaft of tibia of a boy of 10 years.

Photograph *(upper right)* of longitudinal section of tibia shown in radiograph above. Part of the cortex and epiphyseal plate have been destroyed, but the epiphysis is still not invaded.

Photomicrograph (x 70) *(right)* showing an osteogenic sarcoma tissue field in which a considerable amount of calcifying intercellular material has been laid down between the tumor cells.



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Jordan and Grossman; Arch. Surg. 74: 871, 1957

Shingleton, et al; Surgery, 42: 12, 1957

Longmire, Jordan and Briggs; Ann. Surg. 144: 681, 1956

Krane; Am. Pract. and Digest, 8: 1275, 1957

Literature on request.

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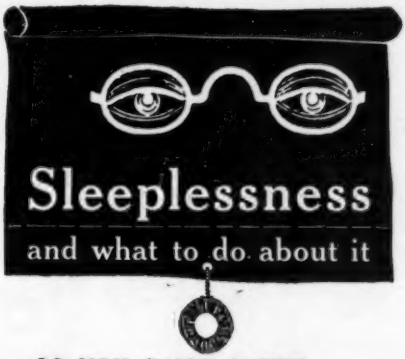

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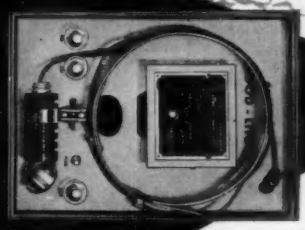

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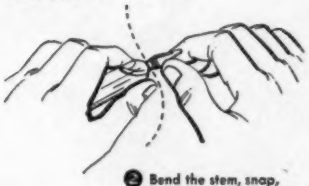

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